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Cancer incidence and cause-specific mortality following Balkan deployment

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This study has been reviewed by a Scientific Advisory Board with Prof. Dr. F.E. van Leeuwen (chairman, The Netherlands Cancer Institute), Dr. L.J. Schouten (Maastricht University) and Prof. Dr. L.A.L.M. Kiemeneij (Radboud University Nijmegen Medical Centre).

This investigation has been performed by order and for the account of the Dutch Ministry of Defence, within the framework of 'Epidemiologisch onderzoek Balkan'.

Abstract

Cancer incidence and cause-specific mortality following Balkan deployment

A study performed by the National Institute for Public Health and the Environment (RIVM) found no association between the deployment of Dutch military personnel in the Balkan region and the incidence of cancer, including leukaemia. There were fewer new cases of cancer and deaths between 1993 and 2008 among Balkan deployed Dutch military personnel than among those who were not deployed to this region. Male military personnel of both groups had a lower chance of developing cancer or dying than men of similar age in the general Dutch population. In 2000, cases of leukaemia among Balkan deployed soldiers were reported in both the international and national media. This study, however, did not identify any increases in the number of cases of leukaemia among Balkan deployed soldiers.

The number of new cases of cancer among the 18,000 men who were deployed to the Balkans was 15% lower than expected based on rates in the general population. The cancer incidence was also lower among Balkan deployed soldiers as compared to the 135,000 soldiers who had not been deployed to the Balkans. The number of lung tumours was half that in the general population, but the underlying factors for this low incidence are unknown as data on smoking habits and other lifestyle factors were not available. The number of leukaemia cases among Balkan deployed military personnel was also lower than expected, but it was not significantly different from the expected number based on the Dutch population. No elevated risk of cancer was observed among the relatively small number of women military personnel who were deployed to the Balkans.

The total number of deaths among soldiers deployed to the Balkans was 33% lower than in the general population on a whole. The mortality rate was also lower among Balkan deployed soldiers than among non-Balkan deployed soldiers. The difference with the general population can be explained by the '*healthy worker effect*' phenomenon that considers the working population, and the military population in particular, to be healthier than the general population on a whole due to health examinations at the time of enlistment and the physical demands of the profession. With regard to causes of death, those due to cancer and to diseases of the circulatory system were particularly lower among Balkan deployed military personnel as compared to the general population.

Keywords:

cancer, deployment, Balkans, military, death

Rapport in het kort

Cancer incidence and cause-specific mortality following Balkan deployment

Er blijkt geen verband te zijn tussen uitzending van militairen naar de Balkan en het optreden van verschillende typen kanker, waaronder leukemie. Het aantal nieuwe gevallen van kanker en het aantal sterfgevallen in de periode 1993-2008 was onder Nederlandse Balkanmilitairen lager dan onder militairen die niet op de Balkan zijn geweest. Zowel de Balkanmilitairen als de niet-Balkanmilitairen hadden een lagere kans op kanker en sterfte vergeleken met even oude mannen uit de Nederlandse bevolking. Dit blijkt uit onderzoek van het RIVM, dat is uitgevoerd naar aanleiding van een vermeend verband tussen uitzending naar de Balkan en het optreden van leukemie.

Het aantal nieuwe gevallen van kanker onder de ruim 18.000 mannen die in de onderzochte periode naar de Balkan zijn uitgezonden, lag in totaal 15 procent lager dan onder even oude mannen uit de Nederlandse bevolking. Het aantal lag ook lager dan onder de 135.000 niet-Balkanmilitairen. Het aantal tumoren in de luchtwegen en borstholte lag de helft lager onder Balkanmilitairen dan onder de Nederlandse bevolking. De reden voor dit lage aantal is onbekend – er waren geen gegevens over roken en andere leefstijlfactoren beschikbaar. Ook het aantal leukemiegevallen lag lager, maar het verschil met de Nederlandse bevolking was niet significant. Voor het relatief kleine aantal vrouwen dat naar de Balkan is uitgezonden, is ook geen verhoogd aantal kankergevallen gevonden.

Het totale aantal sterfgevallen onder Balkanmilitairen in de periode 1993-2008 lag 33 procent lager dan onder even oude mannen uit de Nederlandse bevolking. Het aantal lag ook lager dan onder de 135.000 niet-Balkanmilitairen. Ook de niet-Balkanmilitairen hadden een lager sterftcijfer dan andere Nederlandse mannen. Dit kan verklaard worden met het '*healthy worker effect*': de werkende bevolking, en uitgezonden militairen in het bijzonder, zijn vanwege bijvoorbeeld de selectie op gezondheid door de dienstkeuring gezonder dan de algemene bevolking. Vooral sterfte aan kanker en hart- en vaatziekten lag lager onder Balkanmilitairen dan onder de Nederlandse bevolking.

Trefwoorden:

kanker, uitzending, Balkan, militairen, sterfte

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Summary

Background

In 2000 the international and national lay-press media reported on cases of leukaemia among Balkan deployed soldiers, which some attributed to alleged exposure to depleted uranium (DU), originating from DU-containing ammunition used by NATO (North Atlantic Treaty Organization) Forces. These media reports prompted questions in the Netherlands and other NATO countries about the occurrence of leukaemia, and its relationship with Balkan deployment and DU exposure in particular. Although the NATO reasoned the DU-related health risk to be very low, it was nevertheless recommended that the NATO countries would perform epidemiological studies on cancer among Balkan veterans. This report describes the analyses for the Dutch military population. Although the study originated from concerns about DU exposure, it is important to note that this epidemiological study does not address any specific causative factors such as exposure to DU, but rather explores associations between deployment status and mortality and cancer incidence.

Aim

The aim of this study was to describe the cancer incidence and cause-specific mortality up to 2008 among Dutch military personnel deployed to the Balkans between 1993 and 2001, compared to:

- military personnel who were in service in the same time period but were not deployed to the Balkans; and
- the general Dutch population of comparable age and sex.

Methods

The study population consisted of military personnel who:

- were in service any time between January 1, 1993 and March 1, 2001;
- worked in the Army or Military Police;
- did not return their no-consent form¹;
- did not die during Balkan deployment, because this was a study on post-deployment mortality.

Cancer incidence and mortality data were collected for the years 1993-2008 from the Netherlands Cancer Registry (NCR) of the Association of Comprehensive Cancer Centres (IKNL) and the Dutch causes of death registry of Statistics Netherlands (CBS), respectively. To study differences in mortality and cancer incidence between Balkan- and non-Balkan deployed military personnel, survival analyses (Cox proportional hazard models) were performed with adjustments for age, appointment, rank and branch of military services. Analyses were performed for men and women separately. For the comparison with the Dutch population, observed numbers of deaths and cases of cancer in Balkan deployed personnel were compared with numbers that would be expected in the Balkan deployed personnel based on the age- and sex-specific incidence and mortality rates in the Dutch population in the same time period.

¹ (Ex-)military personnel was given the opportunity to refuse matching their personal data with the Netherlands Cancer Registry and cause of death registry. Only 2% returned their no-consent card.

Results

The study population consisted of 19,167 Balkan deployed and 138,309 non-Balkan deployed persons. The Balkan deployed group included 992 women. The majority (81%) of the non-Balkan deployed military male personnel were conscripts, whereas the Balkan-group included relatively few conscripts (15%). The median age of both groups was 21 years in 1993. The median follow-up time of Balkan deployed military personnel was 11 years.

The total cancer incidence rate among Balkan deployed military men was 17% lower than the cancer incidence rate among non-Balkan deployed military men (hazard ratio (RR) 0.83 (95% confidence interval (CI) 0.69-1.00)). The cancer incidence rate was also lower (15%) as compared to the Dutch male population of comparable age (Standardized Incidence Ratio (SIR)=0.85 (95% CI 0.73-0.99)). For the main cancer sites separately, cancer incidences were similar, with the exception of tumours in the respiratory system and intrathoracic organs, of which the incidence was half that in the Dutch population (SIR=0.48 (95% CI 0.25-0.84)). Also for leukaemia, the observed number (n=5) appeared to be lower than the expected number (n=8), based on the Dutch population, but the difference was not statistically significant. For Balkan deployed women, no significant elevations as compared to non-Balkan deployed women or the Dutch female population were observed either.

The total mortality rate of Balkan deployed military men was 38% lower than the mortality rate of non-Balkan deployed military men (RR=0.62 (95% CI 0.52-0.75)). The mortality rate was also lower (33%) as compared to the Dutch male population of comparable age (Standardized Mortality Ratio (SMR)=0.67 (95% CI 0.57-0.78)). The risk of death from cancer and diseases of the circulatory system was significantly lower in the Balkan deployed group as compared to the Dutch population, whereas death due to other causes was similar in both groups. For Balkan deployed women, the numbers were too small to perform meaningful analyses by cause of death, but the overall mortality appeared to be similar to the expected mortality (SMR 0.74 (95% CI 0.15-2.16)).

The low cancer incidence and mortality rates were not restricted to the Balkan-group; relatively low rates as compared to the Dutch population were observed for the non-Balkan deployed group as well, particularly for mortality. Results were similar in analyses without conscripts.

Conclusion

This study showed that the cancer incidence and all-cause mortality in Balkan deployed men was lower than in non-Balkan deployed men in the study period of 15 years. This study also showed that Dutch military men, Balkan deployed or not, had a lower risk of developing cancer and mortality as compared to the general population of comparable age. For women, no elevated risk of developing cancer following Balkan deployment was observed either.

The results of the present study are in line with results of similar studies regarding cancer in Balkan deployed military personnel in Denmark, Sweden and Italy. Furthermore, the results of this study support the conclusion of a previous report, i.e. that 'it was unlikely that exposure of Dutch soldiers to DU-containing particles during the 1999 Kosovo War would have had a significant health effect', because exposure levels were minimal.

The lower cancer incidence and mortality rate observed in Dutch military men as compared to the Dutch population are generally attributed to a better health and fitness of military personnel because of the health examination at the time of enlistment and the physical demands of the profession. This is known as the 'healthy soldier effect'. A possible explanation for the lower cancer incidence and mortality rate in Balkan deployed vs. non-Balkan deployed military personnel is that those who are ill are less likely to be deployed (the 'healthy warrior effect'). However, the finding of a lower risk of developing tumours in respiratory organs in Balkan deployed military men as compared to the Dutch population was remarkable as it is generally assumed that smoking is more common in the military population than in the general population. Unfortunately, information regarding smoking habits of this population was unavailable.

This study is the largest study in Balkan veterans performed to date, with the longest period of follow-up. However, because of potential long latency times, future effects of deployment on cancer incidence cannot be completely ruled out. For myeloid leukaemia, which has frequently been associated with radiation, however, the latency time is relatively short (5-10 years). Furthermore, health effects by DU-exposure in the Balkan deployed group have previously been reported to be 'unlikely'². Therefore, future health effects are not expected.

² TNO assessed the fate of depleted uranium in the 1999 Kosovo War, potential DU exposure, and the radiological and chemical health risks associated with that among Dutch military personnel deployed to Kosovo (1).

1 Introduction

1.1 Background

In 2000 the international and national lay-press media reported on cases of leukaemia among Balkan deployed soldiers or peacekeepers, which some attributed to alleged exposure to depleted uranium (DU), originating from DU-containing ammunition used by NATO Forces (2). These media reports prompted questions in the Netherlands and other NATO countries about the occurrence of leukaemia, and its relationship with Balkan deployment and DU-exposure in particular (2-4).

In response to the mounting concern in the military and the public, a first preliminary evaluation (the so-called 'quick scan') was made by the Military Medical Service Agency of the Netherlands (3). No indication was found in this quick scan for a higher incidence of leukaemia among Dutch military personnel in active duty in the first eight years following deployment to Kosovo (3). In addition, the Military Medical Service Agency reasoned the DU-related health risk to be very low, based on an estimated level of DU-exposure through inhalation of DU-containing material during the Dutch deployment in Kosovo (3). The Chiefs of Military Medical Services (COMEDS) of the NATO came to similar conclusions in a meeting in January 2001, based on available international data (2) (<http://www.nato.int/du/docu/d010115a.htm>, visited December 24, 2010). In the same COMEDS meeting it was nevertheless recommended that the NATO countries would perform epidemiological studies on cancer among Balkan veterans.

Early 2001, the Dutch ministry of Defence decided to commission two studies by independent bodies (3). Firstly, the Netherlands Organisation for Applied Scientific Research (TNO) performed a desk-top study on depleted uranium in the Kosovo War. TNO assessed the fate of depleted uranium in the 1999 Kosovo War, potential DU-exposure, and the radiological and chemical health risks associated with that among Dutch military personnel deployed to Kosovo (1). It was concluded that, even if a worst-case approach was considered throughout the entire calculation cascade, "it appears to be unlikely that exposure of Dutch soldiers to DU-containing particles during the 1999 Kosovo War would have had a significant health effect" (1).

Secondly, the Dutch National Institute for Public Health and the Environment (RIVM) was commissioned to perform the present epidemiological study (3). RIVM was asked to describe the incidence of cancer and mortality up to 2008 among Dutch military personnel deployed to the Balkans between 1993 and 2001 and their peers. Such comparisons of large cohorts are important to detect any adverse health effects, from whatever cause in a particular deployment (5). It is important to note from the start, however, that this epidemiological study does not address any specific causative factors such as exposure to DU, but rather explores associations between deployment status and mortality and cancer incidence. This is because there was no information available about DU-exposure or any other determinants of health. Therefore, a full review of possible health risks related to (military use of) DU or any other potential natural or man-made hazards attributed to Balkan deployment is beyond the scope of the present study. Those interested in the topic are referred to a number of publications, for example references (1, 6-10).

1.2 Objectives

The aim of this study was to describe the cancer incidence and cause-specific mortality up to 2008 among Dutch military personnel of the Army and Military Police deployed to the Balkans between 1993 and 2001, based on health and mortality registry data. Comparisons were made with military personnel who were in service in the same time period, but who were not deployed to the Balkans, and the general Dutch population of comparable age and sex. Deployments before 1993 were not included because of lack of digitalized historical military data. Deployments after 2001 were not included because of extended latency periods associated with most types of cancer. Personnel of the Navy and Air Force could not be included because of the lack of complete historical data on all military personnel in these branches. Also leukaemia was evaluated, as concerns regarding leukaemia led to this study.

1.3 The Dutch military contribution to Balkan missions

The conflicts at the Balkans started when Croatia and Slovenia declared their independence mid-1991, which resulted in combats with the Yugoslavian Federal Army. The international interference commenced with the 'European Community Monitoring Mission' in 1991, which also involved Dutch military personnel. A number of missions followed, mainly in Bosnia-Herzegovina and Kosovo, when the conflicts spilled over to other regions of the Former Yugoslavia (http://www.defensie.nl/missies/bosnie/waarom_naar_bosnie/, visited November 24, 2010). This study focuses on Dutch deployments for missions in the Balkans between 1993 and 2001 (see chapter 3). According to the Dutch Veteran Registration System of the Ministry of Defence, a total of 25,000 Dutch military (from all branches) were involved in missions on land between 1993 and 2001. Figure 1.1 shows the main Balkan missions in former Yugoslavia in which personnel from the Army and Military Police were involved during this period. After 2001, approximately 8,000 Dutch military personnel were sent to the Balkans.



Figure 1.1. Map of main Balkan missions of the Army and Military Police in former Yugoslavia (including double counting of military personnel if deployed more than once).

1.4 Organization of the report

Chapter two provides a literature review on cancer and mortality in veterans. Chapter three describes the methods of this study, including study design, study population, data collection and data analysis. In chapter 4, the results are described for cancer and mortality separately. The results are discussed in chapter 5, and chapter 6 provides the conclusions which have been drawn based on this study.

2 Previous epidemiological studies on cancer and mortality in veterans

This study focuses on military personnel deployed to the Balkans. Some of the Dutch Balkan (UNPROFOR) veterans have (also) participated in other studies, for example on perceived health (e.g. (11, 12)) or on posttraumatic stress symptoms (e.g. (13, 14)). However, cancer and mortality have not yet been studied in Dutch Balkan veterans. In light of the still limited international literature on Balkan veterans, epidemiological studies on cancer and mortality in relation to military deployment to other wars and peacekeeping missions are also briefly considered here. Most of the previous studies compared a group of military personnel who were deployed to a certain mission to either the general population or to military personnel who were in service in the same period, yet not deployed to that particular mission (a so called Era group). In the present study both these comparisons will be made.

2.1 Previous studies on cancer in veterans

Although the lay-press media suggested a higher leukaemia incidence among Balkan veterans in 2000, to date this has not been confirmed in the international peer-reviewed literature. A recent study in Italy (15) showed a lower cancer incidence than expected in military personnel deployed to Kosovo, Bosnia, and non-deployed personnel, as compared to the general population over the years 1996-2007. However, although this was not the case for the entire study period, the standardized incidence ratio (SIR) was significantly higher than expected in the year 2000 for Hodgkin's lymphoma among troops deployed in Bosnia and non-deployed personnel and in 2001 for thyroid cancer among troops deployed in Bosnia. For the Kosovo group and other years, no such elevations were observed. Therefore, the authors concluded that these findings represented chance findings. These analyses were an update of the provisional analysis performed by the 'Mandelli committee' (see Table 2.1) which was published in a report (not a peer-reviewed publication) (16). Like the Mandelli analysis, the analysis by Peragallo et al. (15) is of limited value because of incomplete collection of cancer cases and non-representative reference data from the general population.

With respect to Balkan veterans from other countries, there are only two epidemiological studies on cancer incidence available in the peer-reviewed scientific literature: one from Sweden (17) and one from Denmark (18). Both studies did not demonstrate an increased incidence of all cancers or leukaemia among Balkan veterans compared to their national rates for the general population of comparable age and sex. It was noted, however, that the follow-up period in these studies (1989-1999 and 1992-2002, respectively) was still short compared to the latency time of cancer development in association with ionising radiation. In another study on post-deployment hospitalisation of US military veterans, comparisons between different cohorts of US active duty military personnel suggested that those who were exclusively deployed to Bosnia were at lower risk of neoplasms compared to those who were exclusively deployed to the Gulf War (19). However, follow-up time in the Bosnia-deployed group was only five years compared to ten years in the Gulf War group, and thus latent disease in the former group might have been inadequately captured.

Others have also studied cancer in Gulf War veterans, which might be of particular relevance here because questions also arose on health risks of exposure to DU from ammunition deployed during the Gulf War. A study on cancer incidence among UK Gulf veterans (Gulf cohort) up to 11 years since the end of the war showed no increased overall or site-specific cancer incidence as compared with service personnel not deployed to the Gulf War back then (20). A report of the US Committee on Gulf War Veterans' Illnesses (21) concluded that depleted uranium was not likely to have caused Gulf War Illness. Instead, use of pyridostigmine bromide pills (given to protect troops from effects of nerve agents) and pesticide use (to combat the region's ubiquitous insect and rodent populations) during deployment were found to be causally associated with this illness. The Committee highlighted the need for information on cancer rates, which have only minimally been assessed in Gulf War veterans so far.

Cancer (incidence, mortality, and hospitalization) has also been studied in military servicemen after other missions by means of various epidemiological approaches. Most of these studies refer to specific exposures attributed to a particular deployment and selected types or sites of cancer, and are therefore not extensively considered here. This concerns, for example, exposure to Agent Orange in Vietnam veterans [e.g. (22-29)], and exposure to ionizing (radioactive) radiation among UK and New Zealand participants in the UK atmospheric nuclear weapon tests in the Pacific between the 1950s and 1960s, e.g. (30, 31).

Table 2.1. Previously reported studies on cancer incidence among UN Balkan veterans.

| | Country | Study design | Outcome | Population | Follow-up/time period | Results (total cancer and leukaemia) (n among Balkan deployed and SIR (95%CI))¹ | Conclusion (authors) |
|-------------------------|----------------|------------------------------------------|-----------------------------------|-------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Storm ea 2006 (18) | Denmark | Population-based historical cohort study | Cancer incidence (registry-based) | Comparison of Danish Balkan deployed military personnel (n=14,012, 13,552 men, 460 women) with the general Danish population | Follow-up period from first Balkan deployment (deployments between 1 Jan, 1992 and 31 Dec, 2001) until death, loss to follow-up or the end of the study (Dec 31, 2002). | Total cancer in men (n=84) 0.9 (0.7-1.1) and in women (n=12) 1.7 (0.9-3.0). Leukaemia in men (n=4) 1.4 (0.4-3.5) and in women (n=0) | 'Cancer incidence is not increased among Danish military personnel deployed to the Balkans.' |
| Gustavsson ea 2004 (17) | Sweden | Population-based historical cohort study | Cancer incidence (registry-based) | Comparison of Swedish Balkan deployed military service personnel (n=8,347 men, 433 women) with the general Swedish population | Follow-up period from first Balkan deployment (involved in UN missions in the Balkans from 1989 to 1999) until death, emigration, a diagnosis of cancer, or the end of the study (Dec 31, 1999). | Total cancer in men (n=26) 1.2 (0.8-1.8) and in women (n=4) 1.5 (0.4-3.9). Chronic myeloid leukaemia in men (n=1) and in women (n=0) | 'Swedish personnel involved in UN missions in the Balkans showed no statistically significantly increased risk of cancer relative to national rates.' '...the period of follow up is too short for an assessment of the long term risk of cancer.' |

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Table 2.1 continued...

| | Country | Study design | Outcome | Population | Follow-up/time period | Results (total cancer and leukaemia) (n among Balkan deployed and SIR (95%CI)) ¹ | Conclusion (authors) |
|------------------------------------------------------------------|---------|-------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 'Mandelli Committee' (16) | Italy | Provisional comparison without taking account of latency time | Detected cancer cases among the Balkan deployed military group and male reference rate in selected regional cancer registries | Comparison of Italian Balkan deployed military and civilian personnel (N=43,058) employed by the Ministry of Defence in the period Dec 1995-2001 and general male population covered in 12 selected Italian regional tumour registries, with data for 1993-1997. | See 'population' (1995-2001). | All tumours (n=44) 0.48 (0.35-0.64). Acute Lymphatic leukaemia (n=2) 1.78 (0.21-6.44) | 1) The overall number of malignant tumours (haematological and otherwise) observed is lower than expected (...). 2) There is a statistically significant excess of Hodgkin's lymphoma (SIR 2.36 (1.22-4.13), n=12) |
| Peragallo et al. 2010 (update of Mandelli Committee report) (15) | Italy | Historical cohort study using number of persons instead of person-years | Cancer incidence based on preliminary army cancer surveillance activity | Comparisons of cancer incidence in military personnel (n=130.275 in 1996 to 40.967 in 2007) deployed in Kosovo, Bosnia and non-deployed personnel. All compared with national pooled incidence rates. | 1996-2007. | Troops (men 20-59 y) deployed firstly in Bosnia all cancers (n=98) 0.48 (0.39-0.59), leukaemia (n=9) 0.99 (0.45-1.87). Troops (men 20-59 y) deployed firstly in Kosovo all cancers (n=66) 0.47 (0.36-0.59), leukaemia (n=5) 0.75 (0.24-1.75). | '... no indication of an increased risk of cancer for Italian soldiers who were stationed in Bosnia and Kosovo. The cluster of Hodgkin's lymphoma in 2000 and of thyroid cancer in 2001 were sporadic events, they did not specifically affect deployed personnel and are unlikely to be related to environmental exposures in the Balkans.' |

1. n=number, SIR=Standardized Incidence Ratio, 95% CI= 95% Confidence Interval

2.2 Previous studies on post-deployment mortality in veterans

There are currently no scientific papers available with respect to post-deployment mortality in Balkan veterans. An epidemiological study among Norwegian former peacekeepers, including Balkan veterans, showed that the overall ('all-cause') and disease-related mortality rates were lower as compared with National figures of the general population of comparable age and sex (SMR 0.85 (0.8-1.0)) between 1978 and 1997 (32). These decreased mortality rates are generally attributed to a better health and fitness of military personnel, which is known as the 'healthy soldier effect' (33). However, in the Norwegian study mortality from external causes such as suicide and motor vehicle accidents was suggested to be higher among these former peacekeepers (32). Nevertheless, a meta-analysis of 12 studies on mortality rates of military personnel showed that compared with the general population, mortality rates from external causes are 10% and 20% lower in deployed and non-deployed military personnel, respectively (33). In comparisons with non-deployed Era military personnel, studies on mortality in US and UK Gulf War veterans consistently showed lower disease-related mortality rates and higher mortality rates from external causes, in particular from (motor vehicle) accidents (34-38). In the present study, therefore, also relative risks of mortality from external causes were calculated.

2.3 Summary

Studies in Italy, Denmark and Sweden do not suggest a higher risk of developing cancer in military personnel deployed to the Balkan region as compared to the general population. These studies had a follow-up period of around 10 years. Elevations of some tumours in the years 2000 and 2001 in some subgroups in Italy were classified as chance findings in a subsequent analysis, because in the whole time span of 11 years the risk of these tumours was not increased. Studies on post-deployment mortality in Balkan veterans are not available so far, but a study among Norwegian peacekeepers showed a lower risk of disease-related mortality as compared to the general population. The present study, described in this report, is unique in the sense that it includes two comparison groups; not only the general population, but also non-deployed military personnel, and because of the relatively long observation period of maximal 15 years.

3 Methods

3.1 Design, study population and data collection

The objectives, mentioned in the introduction, were addressed by performing a historical cohort study, which means that Balkan deployment occurred before the beginning of the study and that military personnel was identified from information that was recorded in the past. Because a central registry of military personnel was lacking, military personnel in service between January 1, 1993 and March 1, 2001 had to be identified from several registers of the Dutch Armed Forces, including employee registers from the Army, Military Police, Air Force and Navy and 'care-for-relatives' records. Available data included:

- Balkan deployment and deployment to other areas, including start and end dates of deployment;
- dates of entrance and termination of service;
- branch of military service;
- rank before and during deployment;
- appointment;
- sex;
- birth year;
- personal details (for data linkages only - see section 3.1.2).

Data of deployments to the Balkans and to other areas were verified using the Netherlands Veteran Registration System (VRS), which was established in 2006. All who had ever been deployed for at least 28 days to the Balkans between 1993 and March 2001 – according to VRS – were included in the 'Balkan deployed' group. Available data in VRS includes for each deployment: name of the mission, mission area, start and end date and rank during the mission.

To check the completeness of the study population, and add military personnel if missing, several additional sources of information were consulted, including staff magazines for changes in the number of employees over the years, salary records and data from the National Civil Pension Fund (in Dutch: ABP).

Addresses, place of birth and follow-up status by January 1, 2008 and personal ID numbers, given to all Dutch citizens (municipal 'A-numbers'), were obtained through the Central Population Registry files by matching on name, birth date and, if necessary, (old) addresses. If matching failed, personal details were checked by sending a letter to the municipality where the person concerned (had) lived. If matching failed for a person who had died, identification through Statistics Netherlands (cause of death registry) was performed. Still, for 3-4% of those who died the cause of death could not be retrieved. Most of these people died while being stationed (not necessarily deployed) abroad, in which case the cause of death was not always registered at Statistics Netherlands. Altogether, almost all of the military personnel (97%) were identified.

3.1.1 Inclusion criteria

The cohort was restricted to people who:

- were in service any time between January 1, 1993 and March 1, 2001;
- worked in the Army or Military Police;
- did not return their no-consent form;
- did not die during Balkan deployment, because this is a study on post-deployment mortality.

The rationale for these criteria was that Balkan deployment started in 1991, but employee records were available from 1993 onwards³. Personnel from the Navy and Air Force could not be included because despite an extensive search for their data, no complete historical employee records could be found for these branches of the military services. However, personnel of the Air Force and most Navy personnel did not execute ground missions, and therefore exposure to DU was unlikely. Civil personnel were excluded, because personnel were militarized when deployed.

3.1.2 *No consent and privacy agreement*

Use of personal data of military personnel was required in this study, to enable matching with the Central (Municipal) Population Registry and the Netherlands Cancer Registry (NCR) of the Association of Comprehensive Cancer Centres (IKNL). The (ex-)military personnel in the cohort was given the opportunity to refuse matching their personal data with the Netherlands Cancer Registry, by sending them a letter describing the study and by asking them to send back a no-consent form if they did not want their registered data to be used in this study (see Appendix 1). Current addresses were obtained by the Central (Municipal) Population Registry. Two percent (3,261 out of 160,737) returned their no-consent form⁴ and were excluded from matching with the Netherlands Cancer Registry and the study as a whole.

Operating procedures for confidential and careful handling of data of those who did not return their no-consent form, were described in detail in a privacy agreement between the Ministry of Defence, the Netherlands Cancer Registry (NCR) and the research institute (RIVM). Central element of this agreement was that none of the involved parties had access to data which was not strictly required for performing the study. The Ministry of Defence, for instance, did not have access to current addresses, cancer incidence and mortality data, the data-analysis unit of RIVM did not have access to any personal data and NCR did not have access to military data (e.g. rank, deployment, appointment). Matching with the anonymous causes of death registry of CBS followed CBS privacy conducts. Analysis of these data took place at CBS hardware, only accessible to two researchers of RIVM by a Remote Access System using fingerprinting. In addition, handling of personal data complied with the Personal Data Protection Act [in Dutch: Wet bescherming persoonsgegevens (Wbp)] and the Municipal Database Act [in Dutch: Wet gemeentelijke basisadministratie persoonsgegevens (Wet GBA)].

3.1.3 *Cancer incidence*

Cancer incidence and mortality data were collected for the years 1993-2008. Using sex, names and birth dates, cross-linkage with the Netherlands Cancer Registry of the Association of Comprehensive Cancer Centres (IKNL) was performed. Addresses and place of birth, and if applicable, date of death, were used to check the matches. The registry contains data on all new cancer cases in the Netherlands; the sensitivity was reported to be 98% (39). Observed cancer cases were extracted from the registry and recoded from ICD-O, which is the Inter-

³ The early missions were restricted to monitoring and there is no information showing that DU was used in the years before 1993.

⁴ Although reasons for refusal were not asked, some persons nevertheless indicated a reason, i.e. written on returned forms. Reasons were not exclusively related to privacy – e.g. some (30% of those who described their reasons) non-Balkan deployed military erroneously returned their form because they had never been deployed to the Balkans.

national Classification of Diseases for Oncology, into the general International Classification of Diseases (ICD-10). As agreed upon in the privacy agreement (section 3.1.2), the IKNL provided year of incidence instead of the exact date of cancer incidence. Benign and non-invasive tumours were excluded, with the exception of non-invasive bladder tumours. Only first cancers were counted. Focus was on the following main cancer site categories (ICD-10 codes in parentheses):

- digestive organs (C15-C26);
- respiratory system and intrathoracic organs (C30-C39);
- urinary tract and genital organs (C60-C68);
- breast (C50);
- haematolymphopoietic system (including leukaemia; C81-C85, C88, C91-C96).

In the comparisons with the Dutch population, all tumours were evaluated separately as well.

3.1.4 *Cause-specific mortality data*

Using unique, anonymous, Dutch personal ID-numbers (municipal 'A-numbers'), cross-linkage with the Dutch causes of death registry of Statistics Netherlands (CBS) by January 1, 2008, was performed. Causes of death were grouped into the 17 main categories of ICD-10, see

<http://apps.who.int/classifications/apps/icd/icd10online/> visited December 24, 2010. The reliability of cause-of-death statistics has been reported to be high (>90%) for the major causes of death (40).

3.2 **Data-analysis**

All statistical analyses were performed using SPSS for Windows version 14.0.

3.2.1 *Differences between Balkan deployed military and their peers*

To study differences in mortality and cancer incidence between Balkan- and non-Balkan deployed military, survival analyses were performed. Cox proportional hazard models were used, in which age was defined as the follow-up variable. Through this, an optimal adjustment for the possible confounding effect of age is obtained. Time under study (follow-up) was included as a time-dependent variable, starting at the beginning of the study (January 1, 1993) or at entrance into duty (if > January 1, 1993) and ending at death, emigration, a diagnosis of cancer or the end of the study (January 1, 2008). Deployment to the Balkans was included as a separate time-dependent variable, depending on end date of the first deployment. Thus, person-time between entrance in the cohort and end of first Balkan deployment was not considered as time at risk of developing cancer or dying, and corresponding person-years were added to the control group, i.e. non-Balkan deployed military personnel. This was done because deaths during deployments were excluded from the study population, and therefore, time at risk of dying could not start before the end of the deployment. For similarity reasons, also time at risk for developing cancer started at the end of the first deployment. Almost always, the duration of deployments was 6 months. Time after end date of first Balkan deployment was counted in the Balkan deployed group, regardless of subsequent deployments to the Balkans or other areas (see Figure 3.1). The analyses provided 'hazard ratios', that is, the ratio between the predicted hazard (i.e. risk of dying or developing cancer) for a member of the Balkan-group and that for a member of the non-Balkan-group, holding everything else constant. Hazard ratios are broadly equivalent to relative risks, a more commonly reported outcome of epidemiological studies, and therefore, will be referred to as relative risks in the results section.

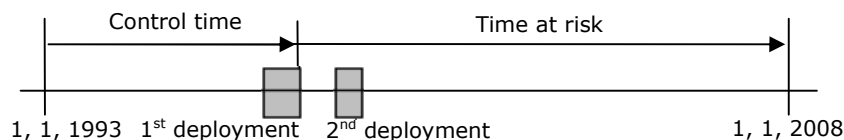


Figure 3.1. Calculation of time at risk for a virtual Balkan deployed soldier who was deployed to the Balkans twice.

All analyses were run for men and women separately. However, the number of women was small, and separate analyses were not always possible. Therefore, the tables of the results section include men only. Results for women are presented in tables in the appendices.

Analyses were adjusted for branch of military service (Army or Military Police), rank (commissioned or non-commissioned officers) and appointment (permanent, temporary or conscription). Chaplains were not considered a separate group but were grouped under 'permanent appointment'. Branch of military service was included as a (crude) indicator of type of work during deployment (and thereby possibly occupational exposures) and rank and appointment as crude measures of socioeconomic status (SES). Adjustment for SES is common in these types of analyses, because there are substantial differences in health and lifestyle across socioeconomic classes, also in the Netherlands (<http://www.nationaalkompas.nl/bevolking/segv/sociaaleconomische-gezondheidsverschillen-samengevat/>, visited November 29, 2010). For example, lower-educated men die, on average, 7 years earlier than higher-educated men. As data on education level and income were not available for the military personnel under study, rank and appointment were used as measures of SES instead.

3.2.2 Standardization to Dutch population

Expected numbers of deaths and cases of cancer in the study population were computed according to the person-year method, based on cause-specific death and cancer incidence rates for the general population in the Netherlands, stratified by age (five year classes), sex and time period (two or three year classes). Standardized mortality (SMR) and incidence rate ratios (SIR) were computed by dividing the observed numbers by the expected numbers. Confidence intervals were calculated using the Poisson distribution. The computational programme for the calculation of SMR and SIR was developed by the Netherlands Cancer Institute, and has been described previously (41). Mortality rates in the Dutch population, from 1993 to 2007, were obtained from Statistics Netherlands. Cancer incidence rates, from 1996 to 2007, were obtained from the Netherlands Cancer Institute (NKI). Cancer incidence rates between 1993 and 1996 were available, but coded according to ICD-9, which does not completely match with coding of some specific tumours in ICD-10 after 1996. Therefore, rates in the Dutch population between 1993 and 1996 were not used. For those cancers which occurred between 1993 and 1996 in the study population (ca. 10%), rates in the Dutch population in 1996 were used as a reference instead.

Standardisation to Dutch population does not provide information on differences between Balkan deployed personnel and their peers

The standardisation to the Dutch population was performed for Balkan and non-Balkan deployed personnel separately. The SMR and SIR cannot be compared across these groups, because this 'indirect' comparison is biased by differences in the distributions of age and other characteristics between these groups. The Cox regression, see section 3.2.1, which provided estimates for Balkan versus non-Balkan deployed personnel, was adjusted for age and some other characteristics. Therefore, results of that analysis provide the best available information on differences across Balkan deployed military and their peers.

3.2.3 *Additional analyses*

All analyses were also conducted without conscripts, because conscription was abolished in August 1996. Also, because conscripts are relatively young, rank may be a less stable indicator for SES in this group (see section 3.2.1). For cancer, analyses without cases occurring within 18 months from the ending date of the mission were performed, as most cancers have a longer latency period. In order to study possible trends over time, SIRs for cancer were calculated separately for the follow-up periods 0-5 years, 5-10 years and 10-15 years.

4 Results

4.1 General characteristics of the study population

The study population included 19,167 persons who had been deployed to the Balkans between 1993 and 2001 (18,175 men and 992 women; 12% of the total study population). The number of non-Balkan deployed military personnel was 138,309, of which 2,954 were women. Of the Balkan deployed military personnel, 928 had also been deployed to other areas. Of the non-Balkan deployed group, 1,308 had been deployed to other areas.

Table 4.1. General characteristics of male military personnel deployed and non-deployed to the Balkans.

| | Balkan deployed¹ (N=18,175) | Non-Balkan deployed (N=135,355) |
|--------------------------------------------------------------------------------------------------------|---------------------------------------------------|--------------------------------------------|
| Median age at January 1, 1993 (p25-p75 ²) | 21 (18-28) | 21 (19-23) |
| Rank (% commissioned officers) ³ | 13.1 | 5.3 |
| Branch (%) | | |
| Army | 94.0 | 94.9 |
| Military Police | 6.0 | 5.1 |
| Appointment (%) | | |
| Permanent | 37.2 | 8.9 |
| Temporary | 47.1 | 10.3 |
| Conscription | 15.3 | 80.8 |
| Other (chaplains) ⁴ | 0.3 | 0.05 |
| Duration of 1 st deployment (median number of days (p25-p75 ²)) ⁵ | 181 (166-185) | - |
| Number of deployments | | |
| 1 (%) | 77.1 | - |
| 2 (%) | 19.1 | - |
| 3 or more (%) | 3.8 | - |

1. All characteristics were significantly different between Balkan vs. non-Balkan deployed military at $p < 0.01$. This was tested by using Chi-Square (sex, rank, appointment, branch of military service) and Wilcoxon statistics (age))
2. 25th and 75th percentiles
3. Rank was available for $n=18,157$ Balkan deployed and 128,077 non-Balkan deployed men
4. Categorised in the analyses as permanent appointment
5. Available for $n=18,155$

Table 4.1 presents general characteristics of Balkan and non-Balkan deployed military personnel. The majority of the non-Balkan deployed military personnel were conscripts working in the Army. Balkan deployed personnel included more commissioned officers and much less conscripts as compared to the non-Balkan deployed military personnel. Most Balkan deployed military personnel worked in the Army. The median age of both groups was 21 years in 1993. Figure 4.1 shows the age distribution of the study population at the start and end of the study period. At the end of the study period, still only 13% of Balkan deployed personnel was older than 50, and 16% between 40 and 50. For non-Balkan deployed personnel, 5% was older than 50 and 5% was between 40 and 50.

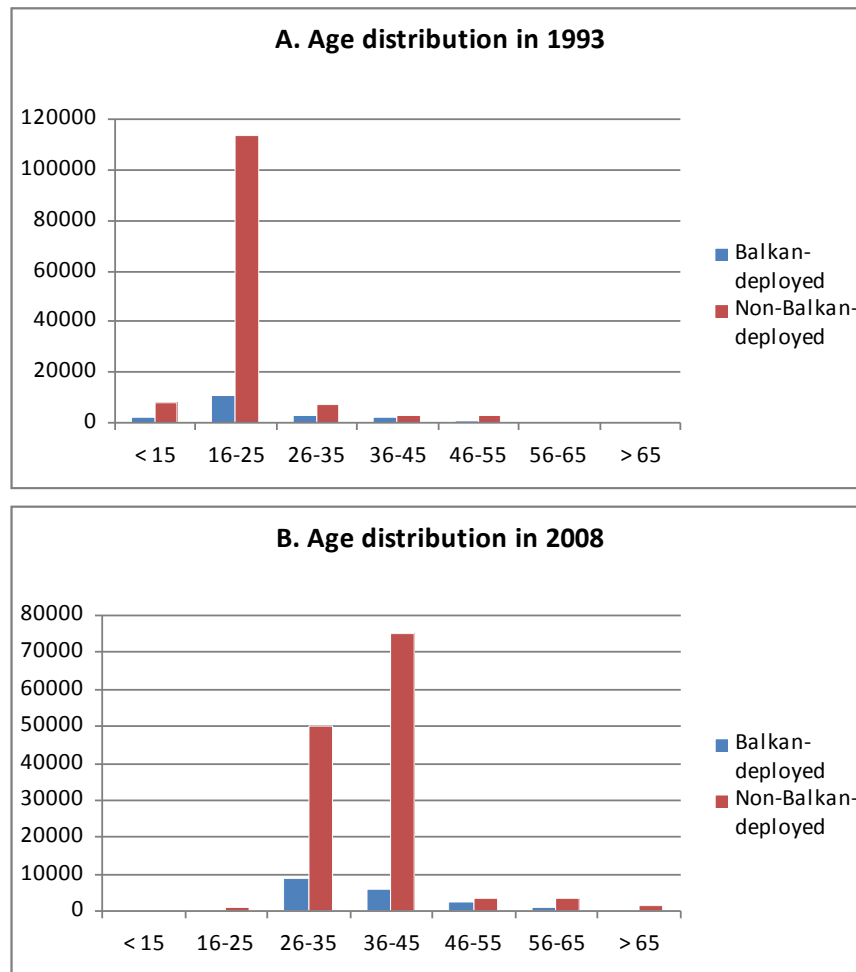


Figure 4.1. Number of military personnel across different age groups among Balkan and non-Balkan deployed military personnel at January 1, 1993 (A) and January 1, 2008 (B).⁵

4.1.1 Characteristics of Balkan deployment

The majority of the Balkan deployed military personnel was deployed only once (77%), but 19% was sent twice and 4% 3 times or more to the Balkans. The median duration of first Balkan deployment was approximately 6 months. Figure 4.2 shows the total number of Balkan deployments over time in the Balkan deployed group.

Table 4.2 gives an overview of the main missions the study population were involved in. The highest numbers of deployments were within SFOR, UNPROFOR, IFOR and KFOR. All missions shown in the table took place in Former Yugoslavia, with the exception of Operation Allied Harbour, which was in Albania. For more details of the missions, see http://www.defensie.nl/nimh/geschiedenis/internationale_operaties/missieoverzicht/, visited December 16, 2010.

⁵ Because some persons were not in military service in 1993, the graphs include persons of less than 15 years of age.

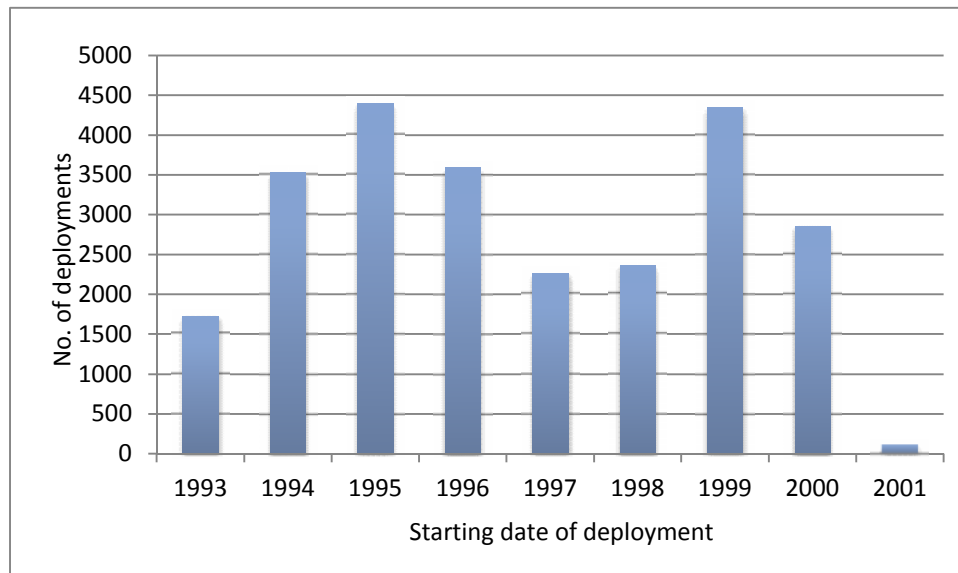


Figure 4.2. Total number of Balkan deployments over time (includes double counting of military personnel if deployed more than once).

Of the non-Balkan deployed personnel, 86% could be followed for at least 10 years and 48% for the complete follow-up time of 15 years. Median follow-up time was 14.8 years. As follow-up of Balkan deployed personnel started later than January 1, 1993, i.e. after the date of first Balkan deployment, 60% could be followed for at least 10 years, but by definition, no one could be followed for the complete follow-up period of 15 years. Median follow-up time for Balkan deployed personnel was 10.9 years.

Table 4.2. Balkan missions of the study population between 1993 and 2001 with at least 50 deployments.

| Mission | Abbreviation | Starting date | End date | Type of mission | No. of deployments¹ |
|--------------------------------------------------------------|--------------------------|----------------------|-----------------|---------------------------------------------------------|---------------------------------------|
| European Community Monitoring Mission | ECMM/EUMM/ EUFOR | 15-07-1991 | 7-1-2007 | Observing | 265 |
| United Nations Protection Force / United Nations Peace Force | UNPROFOR / UNPF | 01-11-1992 | 31-12-1996 | Peacekeeping, observing, peace enforcement (safe areas) | 6,556 |
| Inzet Luchtwapen | DENY FLIG / delib gua | 12-04-1993 | 20-12-1995 | Air Force | 230 |
| Sharp Guard and WEU/Donau | SHARP GUAR /WEU Donau | 15-06-1993 | 27-06-1996 | Embargo Adriatic Sea and Danube | 156 |
| Task Force Mostar | WEU MOSTAR | 01-07-1994 | 31-10-1996 | Peacekeeping | 54 |
| Implementation Force | IFOR | 20-12-1995 | 20-12-1996 | Peace enforcement | 3,232 |
| United Nations Mission in Bosnia and Herzegovina | UNMIBH / UNIPTF | 01-03-1996 | 01-01-2003 | Peacekeeping | 752 |
| Stabilization Force | SFOR | 20-12-1996 | 02-12-2004 | Peace enforcement | 8,370 |
| Extraction Force | EF | 13-02-1999 | 24-03-1999 | Peace enforcement | 120 |
| Operation Allied Force / Allied Harvest | OAF | 24-03-1999 | 20-06-1999 | Combat without UN Mandate | 144 |
| Kosovo Force | KFOR | 12-04-1999 | 08-08-2000 | Peace enforcement | 2,737 |
| Operation Allied Harbour | OAH | 14-04-1999 | 10-07-1999 | Humanitarian intervention | 223 |

1. including double counting of military personnel if deployed more than once

Relative risk (RR) and confidence interval (CI)

The ratio of the absolute risk of cancer or mortality in Balkan deployed military personnel and the absolute risk in non-Balkan deployed military personnel is called the relative risk. If the absolute risk in the former group is higher than the absolute risk in the latter group, the relative risk is higher than 1, and thus Balkan deployed personnel have a greater risk of cancer or mortality.

Due to mere chance the calculated relative risk may differ from the true relative risk. This occurs more often if the number of observations is rather small. Because the true relative risk is unknown, it is common practice to indicate a range of values in which the true relative risk is located with 95% certainty. This range is called the *95%-confidence interval (95% CI)*. If the entire 95% CI is above or below 1, the relative risk is considered to be statistically significantly increased or decreased. However, a statistically significantly increased or decreased relative risk is no guarantee that the finding is no 'chance finding'. If multiple comparisons are made, like in this study, which includes many different tumours for instance, it becomes more likely that only by chance the Balkan-group differs from the other groups for at least one tumour site. This effect has been taken into account in the interpretation of results, by focusing on categories of cancer sites instead of single tumour sites and by disregarding tumours with observed and expected numbers lower than 3.

4.2 Cancer incidence

4.2.1 *Comparison between Balkan deployed military and their peers*

In Balkan deployed men, 175 new cases of cancer were observed up till 2008. In non-Balkan deployed men, 1,337 new cases of cancer were observed. The total cancer incidence rate among Balkan deployed military personnel was lower than the cancer incidence rate among non-Balkan deployed military personnel (relative risk (RR)=0.83 (95% confidence interval (CI) 0.69-1.00; see Figure 4.3). For the 4 main cancer sites separately, cancer incidences were similar in both groups. For breast cancer, numbers were too low for comparisons across groups. The additional analyses without conscripts showed similar results, for example for cancer in total the relative risk was 0.86 (95% CI 0.70-1.05). Twenty cases occurred within 18 months from the ending date of the mission. Results of analyses excluding these cases were similar to the overall results (see Appendix 6).

In Balkan deployed women, 10 cases of cancer were observed and the corresponding relative risk was 1.48 (95% CI 0.69-3.18).

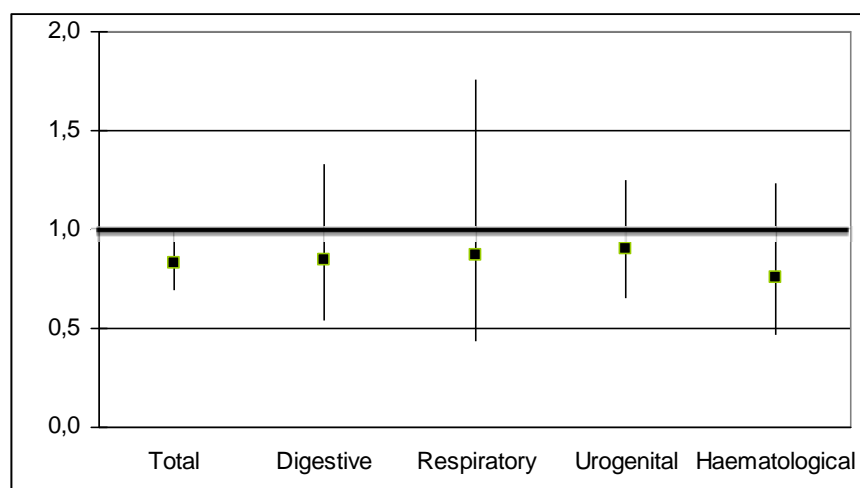


Figure 4.3. Relative risks¹ of total and site-specific incidence of cancer in Dutch male military personnel deployed to the Balkans (N= 18,175) compared with non-Balkan deployed personnel.

¹ Adjusted for rank, appointment and branch of military service.

4.2.2 Comparison between Balkan deployed military and the Dutch population

In men, the observed number of new cancer cases among Balkan deployed military personnel (n=175), was 15% lower than the expected number of cases (n=205), based on the cancer incidence rates in the Dutch population (see Table 4.3). The SIR was close to unity in the first 5 years of follow-up and then declined to 0.65 in the last 5 years of follow-up. For the 4 main cancer sites separately, cancer incidences were similar, with the exception of tumours of the respiratory system and intrathoracic organs, which showed a significantly lower incidence among Balkan deployed military personnel (SIR=0.48 (95% CI 0.25-0.84)) than among the age- and sex-matched Dutch population (see Table 4.3). Most common tumours in this group are bronchus and lung tumours. For leukaemia, the observed number (n=5) appeared to be lower than the expected number (n=8.0), based on the rates in the Dutch population (see Table 4.3).

Among Balkan deployed professional military personnel (i.e. without conscripts; Appendix 4) the SIR for all tumours was 0.87 (95% CI 0.74-1.01) and the SIR for tumours of the respiratory system and intrathoracic organs was 0.49 (95% CI 0.25-0.86). Among non-Balkan deployed military men (Appendix 3) a lower incidence of all tumours (SIR=0.91 (95% CI 0.87-0.96)) and tumours of the respiratory system and intrathoracic organs (SIR=0.64 (95% CI 0.51-0.79)) was observed as compared to the Dutch population. In Balkan- and non-Balkan deployed women, the SIR for all tumours were 1.31 (95% CI 0.63-2.41) and 1.15 (95% CI 0.77-1.64), respectively (Appendix 2).

Table 4.3. Cancer incidence among Dutch military personnel deployed to the Balkans (N= 18,175) as compared to the age- and sex-matched Dutch population.

| Cancer site | ICD-10 codes | Observed | Expected | SIR (95% CI) |
|---------------------------------------------|---------------------|-----------------|-----------------|---------------------|
| All cancers | All | | | |
| total period | | 175 | 205.3 | 0.85 (0.73-0.99) |
| 0-5 y | | 74 | 70.7 | 1.05 (0.82-1.31) |
| 5-10 y | | 74 | 93.3 | 0.79 (0.62-1.00) |
| 10-15 y | | 27 | 41.3 | 0.65 (0.43-0.95) |
| Digestive organs | C15-C26 | | | |
| total period | | 30 | 36.5 | 0.82 (0.56-1.17) |
| 0-5 y | | 7 | 11.1 | 0.63 (0.25-1.30) |
| 5-10 y | | 16 | 17.1 | 0.93 (0.53-1.52) |
| 10-15 y | | 7 | 8.2 | 0.85 (0.34-1.76) |
| Respiratory system and intrathoracic organs | C30-C39 | | | |
| total period | | 12 | 25.0 | 0.48 (0.25-0.84) |
| 0-5 y | | 8 | 8.0 | 1.00 (0.43-1.97) |
| 5-10 y | | 3 | 11.6 | 0.26 (0.05-0.76) |
| 10-15 y | | 1 | 5.5 | 0.18 (0.00-1.01) |
| Bronchus and Lung | C34 | 10 | 20.8 | 0.48 (0.23-0.89) |
| Urinary tract and genital organs | C60-C68 | | | |
| total period | | 55 | 54.1 | 1.02 (0.77-1.32) |
| 0-5 y | | 22 | 17.9 | 1.23 (0.77-1.86) |
| 5-10 y | | 27 | 25.1 | 1.08 (0.71-1.57) |
| 10-15 y | | 6 | 11.2 | 0.54 (0.20-1.17) |

Table continued on next page...

Table 4.3 continued...

| Cancer site | ICD-10 codes | Observed | Expected | SIR (95% CI) |
|----------------------------|---------------------------------|-----------------|-----------------|---------------------|
| Haematolymphopoetic system | C81-C96 (C81-C85, C88, C91-C96) | | | |
| total period | | 28 | 29.3 | 0.95 (0.63-1.38) |
| 0-5 y | | 13 | 11.8 | 1.10 (0.59-1.88) |
| 5-10 y | | 8 | 12.6 | 0.63 (0.27-1.25) |
| 10-15 y | | 7 | 4.9 | 1.43 (0.58-2.96) |
| Leukaemia | C91-C96 | | | |
| total period ¹ | | 5 | 8.0 | 0.63 (0.20-1.46) |

¹ Total number too low to stratify analyses by follow-up period (0-5, 5-10, 10-15 years).

4.3 Mortality

4.3.1 Comparison between Balkan deployed military and their peers

In the total population, 165 deaths were observed during the 15 years of follow-up. The total mortality rate of Balkan deployed military personnel was lower than the mortality rate of non-Balkan deployed military personnel (RR=0.62 (95% CI 0.52-0.75), Figure 4.4). The risk of death from cancer was lower among Balkan deployed military personnel (RR=0.66 (95% CI 0.46-0.97)). Mortality of diseases of the circulatory system and digestive system was similar in both groups. Mortality due to external causes was significantly lower among Balkan deployed than non-Balkan deployed military personnel (RR=0.56 (95% CI 0.42-0.76)). This was mainly caused by fewer fatal transport accidents in Balkan deployed personnel; the risk of suicide was non-significantly lower. For the other main categories of causes of deaths, hazard ratios could not be calculated because of small numbers of deaths.

In professional military personnel only (i.e. without conscripts), results were similar to the results of the overall analyses, for example for all-cause mortality the relative risk was 0.65 (95% CI 0.53-0.79), and for external causes 0.51 (95% CI 0.36-0.72). For Balkan deployed women, the mortality rate was too low to perform analyses.

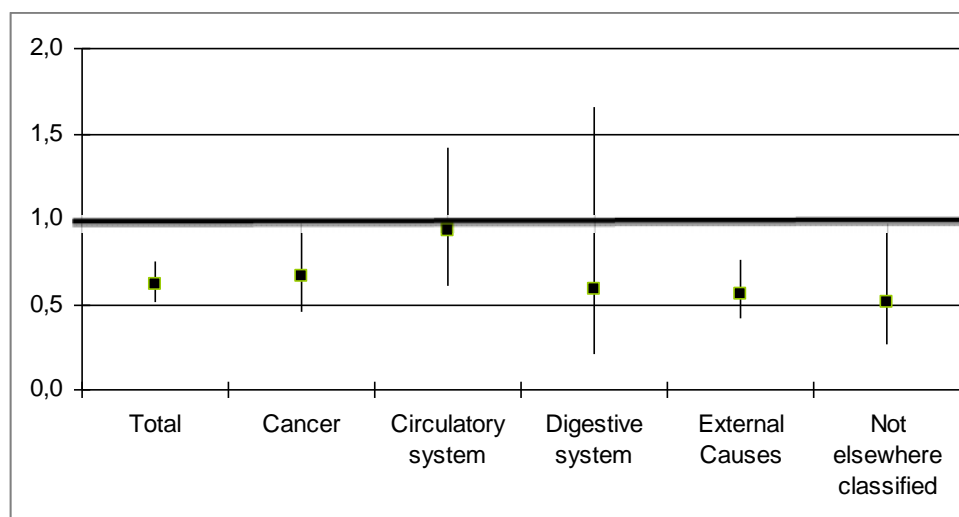


Figure 4.4. Relative risks¹ of mortality² in Dutch military personnel deployed to the Balkans (N= 18,175) compared with non-Balkan deployed personnel during 15 years of follow-up.

¹ Adjusted for rank, appointment and military branch.

² Cox regression could not be performed for other main causes of death, because of low numbers of observed deaths.

4.3.2 Comparison between Balkan deployed military and the Dutch population

Table 4.4 shows cause-specific observed versus expected numbers of deaths and standardized mortality rates (SMRs) for male Balkan deployed military personnel. The observed number of deaths (n=165) after deployment to the Balkans was 33% lower than the expected rate, based on the age- and sex-matched Dutch population (SMR=0.67 (95% CI 0.57-0.78)). The expected top 3 causes of death in a young male population are external causes, cancer and diseases of the circulatory system. This was in line with the observed numbers (same 'top 3') among Balkan deployed military personnel. The risks of mortality

due to cancer (SMR=0.61 (95% CI 0.43-0.82)) and diseases of the circulatory system (0.71 (95% CI 0.50-0.98)) were lower in Balkan deployed personnel than in the Dutch population, whereas the risk of mortality due to external causes was similar in both groups.

In non-Balkan deployed military personnel, the SMR for all causes of death was 0.57 (95% CI 0.54-0.61; Appendix 3). Because of larger numbers of observed cases due to the much larger population, SMRs could be calculated for more main death categories than in Balkan deployed personnel. For all main categories, death rates were lower than the expected rates based on the Dutch population. SMRs ranged from 0.08 for congenital malformations, deformations and chromosomal abnormalities to 0.72 for cancer.

In professional Balkan deployed military personnel, SMRs were similar to those found in the overall analyses (Appendix 4). SMRs for all causes, cancer and diseases of the circulatory system were 0.65 (95% CI 0.55-0.76), 0.59 (95% CI 0.42-0.81) and 0.73 (95% CI 0.51-1.01), respectively. The SMR for external causes of death was 0.85 (95% CI 0.63-1.14). In Balkan deployed women, the number of deaths (n=3) appeared to be similar to the expected number (n=4) (Appendix 2).

Table 4.4. Mortality among Dutch military men deployed to the Balkans (N= 18,175) as compared to the age-matched Dutch male population, summarized in main causes of death categories.

| Cause of death | ICD-10 code | Observed | Expected | SMR (95% CI) |
|-----------------------------------------------------------------------------------------------------|--------------------|-----------------|-----------------|---------------------|
| Total | All | 165 | 246.9 | 0.67 (0.57-0.78) |
| Certain infectious and parasitic diseases | A00-B99 | 1 | 5.0 | 0.20 (0.01-1.10) |
| Cancer | C00-C97 | 41 | 67.7 | 0.61 (0.43-0.82) |
| Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism | D50-D89 | 0 | 0.7 | |
| Endocrine, nutritional and metabolic diseases | E00-E90 | 0 | 6.0 | |
| Mental and behavioural disorders | F00-F99 | 1 | 3.0 | 0.33 (0.01-1.85) |
| Diseases of the nervous system | G00-H95 | 0 | 6.6 | |
| Diseases of the circulatory system | I00-I99 | 36 | 50.6 | 0.71 (0.50-0.98) |
| Diseases of the respiratory system | J00-J99 | 1 | 6.2 | 0.16 (0.00-0.90) |
| Diseases of the digestive system | K00-K93 | 5 | 9.4 | 0.53 (0.17-1.25) |
| Diseases of the skin and subcutaneous tissue | L00-L99 | 0 | 0.2 | |
| Diseases of the musculoskeletal system and connective tissue | M00-M99 | 0 | 0.8 | |
| Diseases of the genitourinary system | N00-N99 | 0 | 1.2 | |
| Pregnancy, childbirth and the puerperium | O00-O99 | 0 | 0 | |
| Certain conditions originating in the perinatal period | P00-P96 | 0 | 0.02 | |
| Congenital malformations, deformations and chromosomal abnormalities | Q00-Q99 | 0 | 2.4 | |
| Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified | R00-R99 | 13 | 18.6 | 0.70 (0.37-1.20) |
| External causes of morbidity and mortality | V01-Y89 | 62 | 66.5 | 0.93 (0.71-1.19) |
| Suicide | X60-X84 | 31 | 28.4 | 1.09 (0.74-1.55) |
| Transport accidents | V01-V99 | 24 | 21.4 | 1.12 (0.72-1.67) |

5 Discussion

5.1 Main findings

This study showed that the cancer incidence and all-cause mortality in Balkan deployed men were lower than in non-Balkan deployed men in the study period of 15 years. This study also showed that Dutch military men, Balkan deployed or not, had a lower risk of developing cancer and mortality as compared to the general population of comparable age. This can be explained by the fact that the working population, and the military population in particular, is healthier than the general population on a whole due to health examinations at the time of enlistment and the physical demands of the profession (see section 5.2). For women, no elevated risk of developing cancer following Balkan deployment was observed either.

The results of the present study are in line with results of similar studies regarding cancer in Balkan deployed military personnel in Denmark, Sweden and Italy (15, 17, 18), see Table 5.1. Furthermore, the results support the conclusion of a previous report, i.e. that 'it was unlikely that exposure of Dutch soldiers to DU-containing particles during the 1999 Kosovo War would have had a significant health effect' (1).

Table 5.1. Results of this study, compared to previous studies on development of cancer following Balkan deployment.

| Study | Obs | Exp | SIR | 95 % CI |
|----------------------|-----|-------|------|-----------|
| Netherlands ('93-08) | 175 | 205.3 | 0.85 | 0.73-0.99 |
| Denmark ('92-01) | 84 | | 0.9 | 0.7-1.1 |
| Sweden ('89-99) | 26 | 21.8 | 1.2 | 0.8-1.8 |
| Italy('96-07) | 164 | 344.9 | 0.48 | 0.39-0.57 |

The sources of the concern about a possible increased risk of cancer following Balkan deployment, which led to this study, were reports in 2000/2001 on an elevated risk of haematological tumours among Balkan deployed personnel in Italy. This elevated risk was attributed to the supposed exposure to depleted uranium. However, a more thorough analysis in 2010 on cancer over a longer time period categorized these findings in Italy as chance findings (15).

5.2 The healthy soldier effect

The lower cancer incidence and mortality observed in the Dutch military personnel can be explained by the so-called 'healthy worker effect'. The healthy worker effect was probably first described by William Ogle at the end of the 19th century (42). It refers to the observation that the working population is healthier than the general population on a whole. Ogle identified two kinds of selection responsible: one working at the time of hire, and the other working throughout employment. The first selectively attracts or rejects new workers depending on physical demands of the job and health selection, by for instance occupational physicians. The second forces people to leave their job because their health is too much impaired for the job they are in. This 'healthy worker effect' is relatively strong for military personnel, due to health examinations at the time of enlistment and the physical demands of the profession. Physical exercise reduces the risk of some site-specific cancers (43) and cardiovascular mortality (44, 45). The risk reduction is at least in part attributed to the favourable effect

of physical activity on the risk factors blood pressure, diabetes mellitus (risk factors for mortality (46)) and obesity (risk factor for mortality (46) and some site-specific cancers (47)). For military personnel, a third selection effect at the time of deployment can be distinguished, as those who are ill are less likely to be deployed (48). Therefore, the 'healthy worker effect' is called the 'healthy soldier effect' or even 'healthy warrior effect' (referring to the third selection effect) in military populations. A meta-analysis of 12 studies showed that the mortality in military populations was 10-25% lower as compared to the general population, depending on cause of death and the period of follow-up (33). Meta-analyses were performed separately for deployed and non-deployed soldiers, resulting in similar estimates of the 'healthy soldier effect' for all-cause and cancer mortality. Figure 5.1 shows the reported pooled meta-standardized mortality ratios for deployed soldiers. The size of the 'healthy soldier effect' in our study was somewhat larger (33% for all-cause mortality, 39% for cancer mortality) than in the meta-analysis (24% and 22% respectively). However, even larger effects have been observed, for instance by Kang et al. (49) in veterans deployed to Iraq and Afghanistan (44% for all-cause mortality, not included in the meta-analysis).

Our study did not only compare Balkan veterans with the general population, but also with their non-deployed peers, which evens out part of the selection effects. The lower mortality and cancer incidence in the Balkan veterans suggested the presence of a 'healthy warrior effect'. Another option would be to compare Balkan deployed personnel with personnel deployed to other areas, i.e. to compare warriors with warriors. However, the number of personnel deployed to other areas between 1993 and 2001 was too low to make this comparison. Further, personnel deployed to other areas has also been exposed to different environmental factors specific to those areas.

In women, relative risks of cancer and mortality were generally higher than in men, and thus there were less indications of a healthy soldier effect in comparisons with the general Dutch, female population. This may be explained by the fact that women without children, who form the majority of the female military personnel, on average have a higher risk of breast cancer than women with children (49). In the Balkan-group in particular, the number of women with children is probably relatively low, because women with young children are not deployed to military missions. However, the higher amount of physical activity in military personnel probably reduces the risk of breast cancer. The overall risk of developing breast cancer in female military populations is not known.

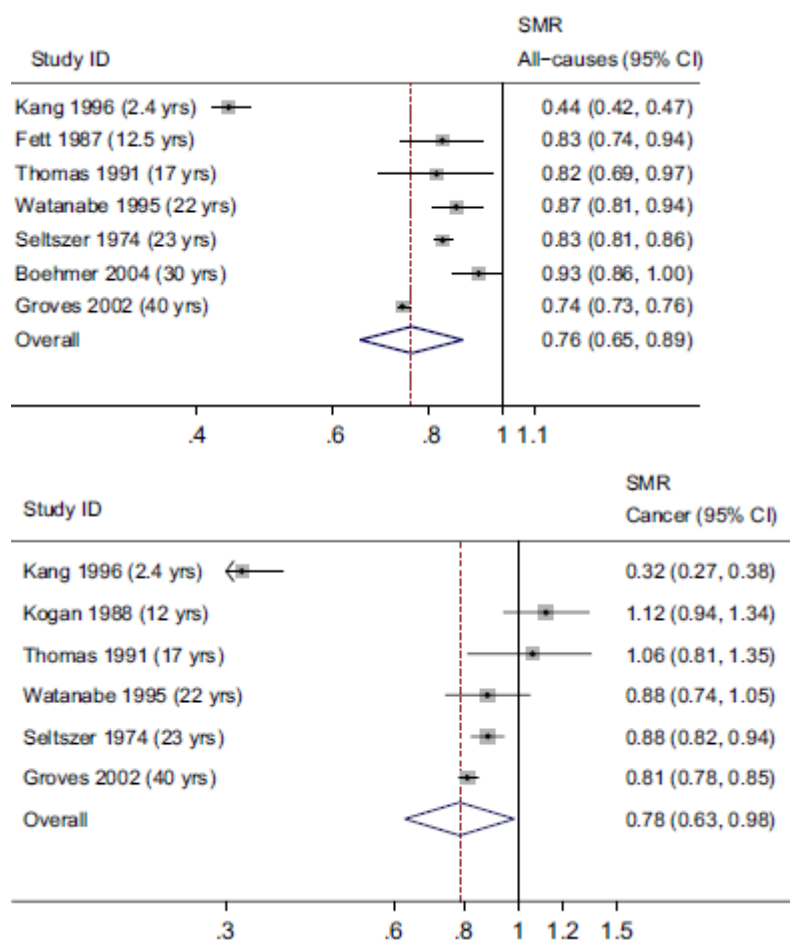


Figure 5.1. Standardized mortality ratios for all causes and for cancer for deployed military personnel, according to the meta-analysis of McLaughlin (33).

5.3 Cause-specific mortality and cancer incidence

Because of the large study population and considerable length of follow-up, this study was not subject to power problems when considering overall mortality and cancer incidence, in the sense that small relative risks remain unnoticed because of low numbers. However, when focusing on rare tumours in subgroups, numbers were limited. In the Balkan deployed group, 5 cases of leukaemia were observed, which appeared to be lower than expected based on the Dutch population ($n=8$), although the difference was not statistically significant. This number was too low to analyze common characteristics of the personnel that developed that disease, but it could be ruled out that they had been involved in one and the same mission in the same time period.

For veterans deployed to the Gulf War, an elevated risk of post-deployment death by external causes, like suicide, and particularly transport accidents as compared to their non-deployed peers has been shown (34-38). In the present study, no such elevations in the deployed compared to the non-deployed group or the Dutch population were found. However, the number of transport accidents was higher in non-deployed, professional military personnel as compared to the Dutch population (see Table A4.2). This finding, which was not observed for the non-deployed group as a whole (see Table A3.1), is actually outside the scope of this study and the underlying factors are unknown. We cannot compare our fin-

dings on mortality in the deployed group with previous studies, as to our knowledge, this is the first study of mortality in a large cohort of Balkan veterans. A modest, but significant increase in the risk of suicide was observed in Norwegian peacekeepers, including Balkan veterans, involved in missions between 1978 and 1995 (32). However, no elevated suicide risks were observed in other studies in peacekeepers (50, 51). Differences in population characteristics, reference groups, time period and deployment-related stressors and hazards might explain the differences in results across studies.

5.4 Lower risk of respiratory tumours

Despite the healthy soldier effect described above, the lower risk of developing tumours in respiratory organs that we found in Balkan deployed military personnel as compared to the Dutch population was against our expectations. Data on smoking habits were not available for this study population, but it was generally assumed that smoking (an important risk factor for respiratory tumours) is more common in the military population than in the general population. A previous study (12) in 1,124 Dutch veterans deployed to some specific areas of the Balkans (Lukavac, Santici and Busovaca) showed that 58% of them smoked during deployment, which is considerably higher than in men of similar age in the general Dutch population

(<http://www.nationaalkompas.nl/gezondheidsdeterminanten/leefstijl/roken/hoeveel-mensen-roken/> visited December 24, 2010). Smoking rates before and after deployment were not reported, but it was stated that 'both current smoking rates and rates during deployment were substantially higher than smoking rates of the Dutch population' (12). However, comparison of smoking rates across studies is complicated, because smoking rates highly depend on the age of the population, the time period and the way smoking habits are assessed. In the United States, relatively high smoking rates have been reported for the military population (52, 53), but a decreasing trend was observed between 1980 and 1998 (54).

Latency time should be taken into account when considering the risk of developing lung cancer, but because it is likely that most smokers in the study population started smoking many years before the onset of the study, an effect of smoking on the development of lung cancer should have been detected.

However, our cohort was relatively young, and lung cancer in men is most observed among 65-80 year olds. Another explanation might be the relatively high amount of physical activity among military personnel. However, despite strong evidence for a protective role of physical activity on cancers of the breast and endometrium, for lung cancer the evidence is weaker (55).

5.5 Completeness of study data

It took a long time to perform this study – nearly 10 years. Most time was spent retrieving and validating historical employment data. This is inherent in the study design, i.e. that data were collected many years after the first deployments, which is common in historical cohort studies which examine the health effects of deployments. Hotopf and Wessely discussed the methodological difficulties associated with this, like tracing the (ex)military population, which is highly mobile because of their job and young age (56). In 2001, each of the 4 branches of military service had its own administration, and each administration had a different format. Deployment data were not recorded centrally either. In addition, records of military personnel who died during active service were removed from the regular administration. It took a long time to build a comprehensive database with data from all different sources, and moreover, to validate

the completeness of the data. Data registry has been much improved in the meantime at the Dutch Ministry of Defence. In 2006, the Veteran Registration System (VRS) was established, which includes detailed data on each mission completed by each veteran. Deployment data collected in 2001 were replaced with the deployment data of the VRS, because the latter had been validated, e.g. by sending letters to veterans. Also, a new employee registry, covering personnel from all branches of service, was established ('PeopleSoft'). Much effort was put into validating the data, e.g. by comparisons with data of the Dutch State Employees' Pension Scheme (ABP). However, the Navy and Air Force could not be included in this study because their data was not complete, e.g. not digitally available for the beginning of the study period. In addition, effects of Balkan deployments before 1993 could not be evaluated. However, there is no information showing that DU-containing ammunition was used in those years, and given the type of the early missions (monitoring) this is unlikely.

In the data-analysis, difficulties in retrieving data were taken into account by performing an analysis restricted to the years after 2001 (see Appendix 5), which was the year of the start of the data collection. Theoretically, people who were in service between 1993 and 2001 and who died during that time period could have been missed because of removal of their data from employee records. However, results of the analysis with the restricted time period were similar to the results over the entire study period, suggesting that the overall results were not biased by missing data on mortality in the early years of follow-up. Bias by missing persons in the cohort because of the no-consent procedure is also unlikely. Only 2% returned their no-consent card and the general characteristics of these persons (rank, appointment, age) were similar to those who were included in the cohort. None of the Balkan veterans returned their no-consent card, and of the non-deployed personnel that returned their card and described a reason for refusal, some (approximately 30%) did so because they thought that Balkan deployment was required to be included in the study, which was not the case. Theoretically, the group who returned their card could differ from the study population with respect to the incidence of cancer, but it is unlikely that this influenced the results, because of the relatively small number of returned cards.

5.6 Methodological issues

The advantage of the long time it took to perform this study was that more years could be added to the follow-up period, resulting in a study period of 15 years. However, as the follow-up started at the end date of the first mission, Balkan veterans have generally been followed for a shorter period of time. Late effects of Balkan deployment on the development of cancer cannot be excluded, as many cancers do not become apparent until 10-20 years after an initiating event. For myeloid leukaemia, however, which has frequently been associated with radiation, the latency time is relatively short. For Japanese A-bomb survivors at the ages of young soldiers, for instance, the incidence peaked at 5-10 years after irradiation (57).

Of note, 'Balkan deployment' is a very crude indicator of potential exposure to uranium and other hazards. Effects might have been 'evened out' because of looking at the entire population instead of focusing on people who were exposed. However, this kind of exposure data was not available. Another limitation of this study is the inability to control for other risk factors for the development of cancer and mortality, such as smoking, alcohol consumption, genetic factors and job history after deployment to the Balkans. If one or more of these risk

factors would show a relationship with Balkan deployment, the observed relative risks may be biased due to confounding. For example, if Balkan deployed personnel had a lower risk of developing cancer because of genetic factors, the potential effects of exposures related to Balkan deployment would have been underestimated. A way to obtain information on confounding variables without the need to question the entire study population would have been to conduct a 'nested' case-control study (58). In such a study additional information on lifestyle factors could have been obtained, which could have been used in the comparisons between Balkan deployed and non-Balkan deployed personnel.

As concluded by Hotopf, epidemiological studies should be planned before military action is contemplated, to avoid difficulties in assessing exposures and health effects afterwards (56). Nevertheless, in the present study several methods were applied to deal with those difficulties. These included adjustment for different sets of potential indicators of socioeconomic status, which did not affect the outcomes of the study. In addition, in contrast to previous studies on Balkan veterans, comparisons with non-deployed personnel were made and not only cancer data, but also mortality data were included.

6 Conclusions

This study showed that the cancer incidence and all-cause mortality in Balkan deployed men was lower than in non-Balkan deployed men in the study period of 15 years. This study also showed that Dutch military men, Balkan deployed or not, had a lower risk of developing cancer and mortality as compared to the general population of comparable age. This can be explained by the fact that the working population, and the military population in particular, is healthier than the general population. Also for women, no elevated risk of developing cancer following Balkan deployment was observed.

This study is the largest study in Balkan veterans performed to date, with the longest period of follow-up. The findings do not change conclusions drawn from previous epidemiological studies – that there are no indications of an elevated risk of developing cancer following Balkan deployment. Furthermore, since health effects by DU-exposure in the Balkan deployed group have previously been reported to be 'unlikely', future health effects are not expected.

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Appendix 1. Letter to participants and no-consent form

2100

Aan



Defensie

Ministerie van Defensie

Hoofddirectie Personeel

Bezoekadres:
Kaivemarkt 32
Postadres:
MPC 58 B
Postbus 20701
2500 ES Den Haag
www.defensie.nl

Datum 23 november 2006

Ons kenmerk P/2006033387

Onderwerp Onderzoek Balkan

Er is onrust ontstaan naar aanleiding van berichtgeving in de media over het voorkomen van medische aandoeningen bij uitgezonden militairen in de Balkan. In opdracht van de Staatssecretaris van Defensie start het RIVM (Rijksinstituut voor Volksgezondheid en Milieu) binnenkort een onderzoek naar de aanwezigheid van kanker en naar sterfte bij personeel van Defensie dat uitgezonden is geweest naar de Balkan. Het aantal patiënten met kanker en overledenen in deze groep zal worden vergeleken met het voorkomen hiervan onder defensiepersoneel dat niet uitgezonden is. Om deze vergelijking te kunnen maken, worden er dus ook brieven verzonden naar (ex) militairen die nooit naar de Balkan zijn uitgezonden. Het onderzoek heeft betrekking op alle (ex)militairen die sinds 1993 in dienst zijn geweest. U hoeft zelf geen informatie te verstrekken, het onderzoek kost u dus geen tijd.

Voor het onderzoek zijn gegevens nodig uit de Nederlandse Kanker Registratie (NKR). Om de gegevens van de juiste personen op te kunnen vragen, verstrekt het Ministerie van Defensie de personalia (naam, geboortedatum, adres) en gegevens inzake het uitzendgebied aan het RIVM. De personalia zullen alleen gebruikt worden voor het opvragen van eventuele gegevens uit de NKR en worden daarna direct verwijderd uit het bestand. Het onderzoeksbestand en het onderzoeksrapport bevatten geen gegevens welke tot personen herleidbaar zijn (geanonimiseerd). De onderzoekers van het RIVM en het Ministerie van Defensie kunnen dus niet achterhalen welke persoonsgegevens horen bij patiënten waarbij kanker is vastgesteld.

Heeft u, ondanks bovengenoemde waarborgen voor de vertrouwelijke omgang met uw gegevens, toch bezwaar tegen het opvragen van uw eventuele gegevens bij de NKR, dan verzoeken wij u om bijgaande antwoordkaart in te vullen en **binnen drie weken na de dagtekening van deze brief** te retourneren.

U dient de kaart dus alléén in te sturen als u niet aan het onderzoek wenst deel te nemen.

Voor nadere informatie en eventuele vragen gaat u naar de website: www.cdc.nl. Vervolgens kiest u bij 'selecteer bedrijf' Bedrijfsgroep Gezondheidszorg. In het menu aan de linkerkant kiest u CEMG en vervolgens Balkan-onderzoek. U kunt ook rechtstreeks het volgende adres gebruiken: www.cdc.nl/mqfb/cemg/balkan.

Mocht u nog vragen hebben, dan kunt u op werkdagen van 9.30 uur tot 12.00 uur bellen naar: **070-3396222**.

Wij hopen op uw medewerking, zodat in het belang van alle betrokkenen inzicht ontstaat in de mogelijke gevolgen van een uitzending.

Met vriendelijke groeten,

De Piv. Hoofddirecteur Personeel



J.G.A. Leijh
Generaal-majoor

Bij beantwoording datum, ons kenmerk en onderwerp vermelden.



ANTWOORDKAART
SVP RETOUR VOOR 30-09-2006

Naam

Telefoonnummer

Maakt bezwaar tegen het opvragen van zijn/haar eventuele gegevens
bij de Nederlandse Kanker Registratie

Handtekening:

geen postzegel
nodig

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Appendix 2. Analyses in women

Table A2.1. Mortality among Dutch military women deployed to the Balkans (N= 992) as compared to the age-matched Dutch female population.

| Cause of death | ICD-10 code | Obs | Exp | SMR (95% CI) |
|-----------------------|--------------------|------------|------------|---------------------|
| Total | All | 3 | 4.1 | 0.74 (0.15-2.16) |

Table A2.2. Mortality among Dutch military women non-deployed to the Balkans (N= 2,954) as compared to the age-matched Dutch female population.

| Cause of death | ICD-10 code | Obs | Exp | SMR (95% CI) |
|--------------------------------------------|--------------------|------------|------------|---------------------|
| Total | All | 17 | 15.6 | 1.09 (0.63-1.74) |
| External causes of morbidity and mortality | V01-Y89 | 8 | 3.8 | 2.10 (0.91-4.14) |
| Suicide ⁶ | X60-X84 | 2 | 1.7 | |
| Transport accidents | V01-V99 | 5 | 1.2 | 4.17 (1.35-9.72) |

Table A2.3. Incidence of cancer among Dutch military women deployed to the Balkans (N= 992) as compared to the age-matched Dutch female population.

| Type of cancer | ICD-10 code | Obs | Exp | SIR (95% CI) |
|-----------------------|--------------------|------------|------------|---------------------|
| Total | All | 10 | 7.6 | 1.31 (0.63-2.41) |
| Breast | C50 | 3 | 2.5 | 1.19 (0.24-3.48) |

⁶ SMR not calculated because of low numbers (observed and expected lower than 3)

Table A2.4. Incidence of cancer among Dutch military women non-deployed to the Balkans (N=2,954) as compared to the age-matched Dutch female population.

| Type of cancer | ICD-10 code | Obs | Exp | SIR (95% CI) |
|-----------------------|--------------------|------------|------------|---------------------|
| Total | All | 30 | 26.2 | 1.15 (0.77-1.64) |
| Breast | C50 | 12 | 8.1 | 1.48 (0.77-2.59) |
| Melanome of skin | C43 | 6 | 4.6 | 1.30 (0.48-2.82) |

Appendix 3. Analyses in men non-deployed to the Balkans

Table A3.1. Mortality among Dutch military men non-deployed to the Balkans (N= 135,355) as compared to the age-matched Dutch male population, summarized in main causes of death categories, lifting out suicide and transport accidents.

| Cause of death | ICD-10 code | Obs | Exp | SMR (95% CI) |
|-----------------------------------------------------------------------------------------------------|--------------------|------------|------------|---------------------|
| Total | All | 1,080 | 1,890.5 | 0.57 (0.54-0.61) |
| Certain infectious and parasitic diseases | A00-B99 | 11 | 39.9 | 0.28 (0.14-0.49) |
| Cancer | C00-C97 | 305 | 423.3 | 0.72 (0.64-0.81) |
| Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism | D50-D89 | 3 | 5.7 | 0.53 (0.11-1.54) |
| Endocrine, nutritional and metabolic diseases | E00-E90 | 10 | 38.6 | 0.26 (0.12-0.48) |
| Mental and behavioural disorders | F00-F99 | 7 | 18.0 | 0.39 (0.16-0.80) |
| Diseases of the nervous system | G00-H95 | 15 | 52.7 | 0.28 (0.16-0.47) |
| Diseases of the circulatory system | I00-I99 | 183 | 315.9 | 0.58 (0.50-0.67) |
| Diseases of the respiratory system | J00-J99 | 14 | 44.5 | 0.31 (0.17-0.53) |
| Diseases of the digestive system | K00-K93 | 25 | 53.6 | 0.47 (0.30-0.69) |
| Diseases of the skin and subcutaneous tissue ⁷ | L00-L99 | 1 | 1.1 | |
| Diseases of the musculoskeletal system and connective tissue | M00-M99 | 3 | 6.1 | 0.49 (0.10-1.44) |
| Diseases of the genitourinary system | N00-N99 | 4 | 7.9 | 0.50 (0.14-1.29) |
| Pregnancy, childbirth and the puerperium | O00-O99 | 0 | 0 | |
| Certain conditions originating in the perinatal period | P00-P96 | 0 | 0.1 | |
| Congenital malformations, deformations and chromosomal abnormalities | Q00-Q99 | 2 | 23.9 | 0.08 (0.01-0.30) |
| Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere | R00-R99 | 94 | 152.1 | 0.62 (0.50-0.76) |

⁷ SMR not calculated because of low numbers (observed and expected lower than 3)

| Cause of death | ICD-10 code | Obs | Exp | SMR (95% CI) |
|--------------------------------------------|--------------------|------------|------------|---------------------|
| classified | | | | |
| External causes of morbidity and mortality | V01-Y89 | 381 | 690.2 | 0.55 (0.50-0.61) |
| Suicide | X60-X84 | 140 | 272.5 | 0.51 (0.43-0.61) |
| Transport accidents | V01-V99 | 178 | 252.3 | 0.71 (0.61-0.82) |

Table A3.2. Incidence of cancer among Dutch military men non-deployed to the Balkans (N=135,355) as compared to the age-matched Dutch male population, summarized in cancer categories.

| Type of cancer | ICD-10 code | Obs | Exp | SIR (95% CI) |
|------------------------|------------------------------|------------|------------|---------------------|
| Total | All | 1,337 | 1,463.1 | 0.91 (0.87-0.96) |
| Digestive organs | C15-26 | 168 | 203.6 | 0.83 (0.71-0.96) |
| Respiratory organs | C30-39 | 86 | 135.2 | 0.64 (0.51-0.79) |
| Urogenital organs | C60-68 | 464 | 429.5 | 1.08 (0.98-1.18) |
| Haematological tumours | C81-C96 (C81-85, C88 C91-96) | 194 | 237.4 | 0.82 (0.71-0.94) |

Appendix 4. Analyses without conscripts

Table A4.1. Mortality among Dutch professional military men deployed to the Balkans (N= 15,387) as compared to the age-matched Dutch male population, summarized in main causes of death categories, lifting out suicide and transport accidents.

| Cause of death | ICD-10 code | Obs | Exp | SMR (95% CI) |
|-----------------------------------------------------------------------------------------|--------------------|------------|------------|---------------------|
| Total | All | 144 | 222.4 | 0.65 (0.55-0.76) |
| Cancer | C00-C97 | 38 | 64.3 | 0.59 (0.42-0.81) |
| Diseases of the circulatory system | I00-I99 | 35 | 48.1 | 0.73 (0.51-1.01) |
| Diseases of the digestive system | K00-K93 | 5 | 8.9 | 0.56 (0.18-1.32) |
| Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified | R00-R99 | 12 | 16.4 | 0.73 (0.38-1.28) |
| External causes of morbidity and mortality | V01-Y89 | 46 | 53.9 | 0.85 (0.63-1.14) |
| Suicide | X60-X84 | 26 | 23.5 | 1.11 (0.72-1.62) |
| Transport accidents | V01-V99 | 15 | 16.6 | 0.90 (0.51-1.49) |

Table A4.2. Mortality among Dutch professional military men non-deployed to the Balkans (N=26,029) as compared to the age-matched Dutch male population, summarized in main causes of death categories, lifting out suicide and transport accidents.

| Cause of death | ICD-10 code | Obs | Exp | SMR (95% CI) |
|-----------------------------------------------|--------------------|------------|------------|---------------------|
| Total | All | 661 | 793.1 | 0.83 (0.77-0.90) |
| Certain infectious and parasitic diseases | A00-B99 | 7 | 16.7 | 0.42 (0.17-0.86) |
| Cancer | C00-C97 | 214 | 268.9 | 0.80 (0.69-0.91) |
| Endocrine, nutritional and metabolic diseases | E00-E90 | 4 | 20.6 | 0.19 (0.05-0.50) |
| Mental and behavioural disorders | F00-F99 | 4 | 9.0 | 0.44 (0.12-1.13) |
| Diseases of the nervous system | G00-H95 | 11 | 18.0 | 0.61 (0.31-1.10) |
| Diseases of the circulatory system | I00-I99 | 132 | 199.2 | 0.66 (0.55-0.79) |
| Diseases of the respiratory system | J00-J99 | 11 | 25.9 | 0.42 (0.21-0.76) |

| Cause of death | ICD-10 code | Obs | Exp | SMR (95% CI) |
|-----------------------------------------------------------------------------------------|-------------|-----|-------|------------------|
| Diseases of the digestive system | K00-K93 | 24 | 30.3 | 0.79 (0.51-1.18) |
| Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified | R00-R99 | 49 | 53.7 | 0.91 (0.68-1.21) |
| External causes of morbidity and mortality | V01-Y89 | 186 | 130.0 | 1.43 (1.23-1.65) |
| Suicide | X60-X84 | 60 | 53.7 | 1.12 (0.85-1.44) |
| Transport accidents | V01-V99 | 100 | 43.5 | 2.30 (1.87-2.79) |

Table A4.3. Incidence of cancer among Dutch professional military men deployed to the Balkans (N=15,387) as compared to the age-matched Dutch male population, summarized in cancer categories.

| Type of cancer | ICD-10 code | Obs | Exp | SIR (95% CI) |
|------------------------|-------------------------------|-----|-------|------------------|
| Total | All | 162 | 187.1 | 0.87 (0.74-1.01) |
| Digestive organs | C15-26 | 29 | 35.1 | 0.83 (0.55-1.19) |
| Respiratory organs | C30-39 | 12 | 24.5 | 0.49 (0.25-0.86) |
| Urogenital organs | C60-C68 | 53 | 48.1 | 1.10 (0.83-1.44) |
| Haematological tumours | C81-C96 (C81-85, C88, C91-96) | 22 | 25.6 | 0.86 (0.54-1.30) |

Table A4.4. Incidence of cancer among Dutch professional military men non-deployed to the Balkans (N=26,029) as compared to the age-matched Dutch male population, summarized in cancer categories.

| Type of cancer | ICD-10 code | Obs | Exp | SIR (95% CI) |
|------------------------|------------------------------|-----|-------|------------------|
| Total | All | 649 | 663.9 | 0.98 (0.90-1.06) |
| Digestive organs | C15-26 | 132 | 139.8 | 0.94 (0.79-1.12) |
| Respiratory organs | C30-39 | 69 | 110.7 | 0.62 (0.48-0.79) |
| Urogenital organs | C60-68 | 213 | 175.3 | 1.22 (1.06-1.39) |
| Haematological tumours | C81-C96 (C81-85, C88 C91-96) | 81 | 73.9 | 1.10 (0.87-1.36) |

Appendix 5. Standardized mortality and cancer incidence ratios with follow-up starting in 2001

Table A5.1. Mortality among Dutch military men deployed to the Balkans (N= 18,175) after 2001 as compared to the age-matched Dutch male population, summarized in main causes of death categories, lifting out suicide and transport accidents.

| Cause of death | ICD-10 code | Obs | Exp | SMR (95% CI) |
|-----------------------------------------------------------------------------------------|--------------------|------------|------------|---------------------|
| Total | All | 117 | 170.7 | 0.69 (0.57-0.82) |
| Cancer | C00-C97 | 31 | 50.7 | 0.61 (0.42-0.87) |
| Diseases of the circulatory system | I00-I99 | 25 | 36.7 | 0.68 (0.44-1.01) |
| Diseases of the digestive system | K00-K93 | 3 | 6.9 | 0.44 (0.09-1.27) |
| Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified | R00-R99 | 9 | 12.1 | 0.74 (0.34-0.41) |
| External causes of morbidity and mortality | V01-Y89 | 42 | 40.3 | 1.04 (0.75-1.41) |
| Suicide | X60-X84 | 19 | 18.6 | 1.02 (0.62-1.60) |
| Transport accidents | V01-V99 | 17 | 11.0 | 1.54 (0.90-2.47) |

Table A5.2. Mortality among Dutch military men non-deployed to the Balkans (N= 135,355) after 2001 as compared to the age-matched Dutch male population, summarized in main causes of death categories, lifting out suicide and transport accidents.

| Cause of death | ICD-10 code | Obs | Exp | SMR (95% CI) |
|-----------------------------------------------------------------------------------------|--------------------|------------|------------|---------------------|
| Total | All | 678 | 982.9 | 0.69 (0.64-0.74) |
| Cancer | C00-C97 | 218 | 254.3 | 0.86 (0.75-0.98) |
| Diseases of the circulatory system | I00-I99 | 120 | 187.3 | 0.64 (0.53-0.77) |
| Diseases of the digestive system | K00-K93 | 16 | 32.5 | 0.49 (0.28-0.80) |
| Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified | R00-R99 | 62 | 72.2 | 0.86 (0.66-1.10) |
| External causes of morbidity and mortality | V01-Y89 | 207 | 296.9 | 0.70 (0.61-0.80) |
| Suicide | X60-X84 | 92 | 133.7 | 0.69 (0.55-0.84) |
| Transport accidents | V01-V99 | 74 | 82.7 | 0.89 (0.70-1.12) |

Table A5.3. Incidence of cancer among Dutch military men deployed to the Balkans (N=18,175) after 2001 as compared to the age-matched Dutch male population, for the total number and haematological tumours.

| Type of cancer | ICD-10 code | Obs | Exp | SIR (95% CI) |
|------------------------|-------------------------------|------------|------------|---------------------|
| Total | | 128 | 154.7 | 0.83 (0.69-0.98) |
| Haematological tumours | C81-C96 (C81-85, C88, C91-96) | 20 | 20.8 | 0.96 (0.59-1.48) |

Appendix 6. Hazard ratios of cancer incidence excluding cases in the first 18 months

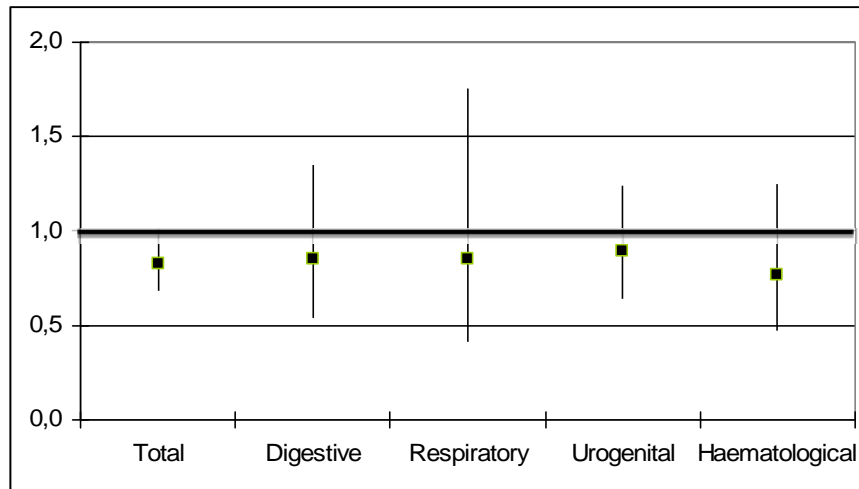


Figure A6.1. Relative risks¹ of total and site-specific incidence of cancer in Dutch male military personnel deployed to the Balkans (N= 18,175) compared with non-Balkan deployed personnel, excluding cases in the first 18 months.

¹ Adjusted for rank, appointment and military branch.

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