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Cancer incidence in Dutch Balkan veterans

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ABSTRACT

Suspicion has been raised about an increased cancer risk among Balkan veterans because of alleged exposure to depleted uranium. The authors conducted a historical cohort study to examine cancer incidence among Dutch Balkan veterans. Male military personnel (n = 18,175, median follow-up 11 years) of the Army and Military Police who had been deployed to the Balkan region (1993–2001) was compared with their peers not deployed to the Balkans (n = 135,355, median follow-up 15 years) and with the general Dutch population of comparable age and sex. The incidence of all cancers and 4 main cancer subgroups was studied in the period 1993–2008. The cancer incidence rate among Balkan deployed military men was 17% lower than among non-Balkan deployed military men (hazard ratio 0.83 (95% confidence interval 0.69, 1.00)). For the 4 main cancer subgroups, hazard ratios were statistically non-significantly below 1. Also compared to the general population cancer rates were lower in Balkan deployed personnel (standardised incidence rate ratio (SIR) 0.85 (0.73, 0.99). The SIR for leukaemia was 0.63 (0.20, 1.46). The authors conclude that earlier suggestions of increased cancer risks among veterans are not supported by empirical data. The lower risk of cancer might be explained by the 'healthy warrior effect'.

1. Introduction

In 2000 the international lay-press reported on cases of leukaemia among soldiers or peacekeepers who had been deployed to the Balkans, i.e. former Yugoslavia. A suspected cause was alleged exposure to depleted uranium (DU), a radioactive and chemically toxic material originating from DU-containing ammunition used by NATO (North Atlantic Treaty Organisation) Forces. The media reports prompted questions in various NATO countries about the occurrence of leukaemia and its relationship with Balkan deployment and DU-exposure in particular. It was therefore recommended by the Committee of the Chiefs of Military Medical Services in NATO (COMEDS) that the NATO countries would study cancer risk among Balkan veterans [1].

Studies from Italy [2], Sweden [3], and Denmark [4] did not demonstrate a higher than expected risk of all cancers including leukaemia among Balkan veterans compared to the general population. However, the follow-up periods in these studies of about 10 years were still short considering the latency time of cancer development by ionising radiation. In addition, since lifestyle factors between the military and general population differ [5], the results of these studies were not convincing and suspicions remained. The present study includes an additional comparison group of non-deployed military, has a large study population, and uses a longer observation period of maximal 15 years.

Others have 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 [6]. A report of the US Committee on Gulf War Veterans' Illnesses [7] concluded that depleted uranium was not likely to have caused Gulf War Illness.

The aim of the present study was to describe cancer incidence including haematological malignancies up to 2008 among Dutch military personnel deployed to the Balkans between 1993 and

Abbreviations: 95% CI, 95% confidence interval; DU, depleted uranium; HR, hazard ratio; NATO, North Atlantic Treaty Organisation; SIR, standardised incidence rate ratio; n, number.

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2001. This epidemiological study does not address any specific causative factors, such as exposure to DU, but provides evidence intended to evaluate public health and policy concerns. Comparisons were made with a cohort of military personnel who were in service during the same time period but who were not deployed to the Balkans. We also compared cancer incidence in Balkan deployed military personnel with the general population of comparable age and sex.

2. Materials and methods

2.1. Study design

The study was a historical cohort study, i.e. deployment of military personnel was identified from information recorded in the past. Cancer incidence rates in the period 1993–2008 were obtained through record linkage with the national cancer registry, and rates in Balkan-deployed personnel were compared with rates in personnel not deployed to the Balkans and the general Dutch population of comparable sex and age.

2.2. Study population

The cohort was restricted to men who were in service any time between January 1, 1993 and March 1, 2001, who worked in the Army or Military Police. Personnel from the Navy and Air Force could not be included because complete historical employee records were not available. However, since personnel of the Air Force and most Navy personnel were only minimally involved in ground missions, exposure to DU was unlikely. Civil personnel was excluded. The (ex-)military personnel could refuse to participate by sending back a no-consent form. Ninety-seven percent of all military personnel could be traced, and 2% of them (3261 out of 160 737) returned their no-consent form. Women (n = 3946) were excluded because the number of women was too small to perform meaningful analyses. The final cohort included 153 530 men.

All men ever been deployed for at least 28 days to the Balkans between 1993 and March 2001 were included in the 'Balkan deployed' group (n = 18,175). Those deployed for less than 28 days were included in the reference population in order to exclude short working visits. Those who died during Balkan deployment were excluded, because the study question concerns post-deployment cancer incidence. The first deployments to the Balkans started in 1991, but employee records were only available from 1993 onwards. However, there is no information showing that DU-containing ammunition was used in the Balkans before 1993, and given the type of the early missions (monitoring), exposure to DU is unlikely. Moreover, the number of deployed personnel before 1993 is considered to be small.

2.3. Data sources

Available data included dates of entrance into service and termination of service, branch of military service, rank, appointment, deployments (name of mission, start- and end date), sex, year of birth, and personal details (for record linkages only – see below). Cancer incidence data were collected for the years 1993–2008 from the Netherlands Cancer Registry (NCR) held by the Association of Comprehensive Cancer Centres (IKNL&IKZ).

2.4. Record linkage with cancer incidence registry

Addresses, place of birth and vital status by January 1, 2008 and unique, anonymous, Dutch personal ID numbers given to all Dutch citizens (municipal 'A-numbers') were obtained through record linkage with the Computerised Municipal Population Registry using name, birth date and, if necessary, (old) addresses as identifiers.

Using sex, name and date of birth, record linkage with the NCR (http://www.kankerregistratie.nl) 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 of record linkage has been reported to be 98% [8]. Observed cancer cases were extracted from the registry and recoded from the International Classification of Diseases for Oncology (ICD-O) into the general International Classification of Diseases (ICD-10). Only invasive cancers were included, as well as non-invasive bladder cancers. Only the first primary cancers were included for incidence determination, because subsequent cancers can be caused by treatment of the first primary. Because modest numbers of cancer cases were expected, cancer types were categorised into large cancer subgroups. The following main cancer subgroups were studied (ICD-10 codes in parentheses):

- digestive organs (C15–C26);
- respiratory system and intrathoracic organs (C30–C39);
- bronchus and lung (C34);
- urinary tract and genital organs (C60–C68);
- haematolymphopoetic system (including leukaemia; C81–C85, C88, C91–C96);
- leukaemia (C91–C96).

The classification we used is a standard one when not enough cases of individual cancer sites are observed to examine cancer risks for all individual organs and tissues separately. We categorised the sites according to tracts (digestive tract, respiratory tract, urogenital tract) or tissues (haematolymphopoetic system), which is often done in epidemiologic studies because the etiologic factors for sites within a tract are assumed to be more similar. Lung cancer was considered separately because of specific concerns about lung cancer in relation to inhaled DU.

2.5. Data analysis

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

2.5.1. Differences between Balkan deployed military and their peers
Differences in characteristics between Balkan- and non-Balkan deployed personnel were tested with a Chi-square or Wilcoxon test, as appropriate. To study differences in cancer incidence between Balkan- and non-Balkan deployed military, proportional hazard models were used with age defined as a follow-up variable. Time under study (follow-up) was included as a time-dependent variable. In this way, differences in follow-up time between groups were taken into account. Time under study started at the beginning of the study (January 1, 1993) or at entrance into duty (if > January 1, 1993) and ended at death, emigration, 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 first deployment. Thus, person-time and cases between entrance in the cohort and end of first Balkan deployment contributed to the non-Balkan deployed group (see Fig. 1).

Analyses were adjusted for branch of military service (Army or Military Police), rank (commissioned or non-commissioned officers) and appointment (permanent, temporary or conscription). Branch of military service was included as a (crude) proxy of type of work during deployment (and thereby possibly occupational exposures). Military rank and type of appointment were used as crude measures of socioeconomic status in the proportional hazard models. Those with missing information on any of