Mortality from multiple sclerosis in British military personnel

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Abstract

Background—While analysing trends in occupational mortality in England and Wales, we noticed an unexpectedly elevated proportion of deaths from multiple sclerosis (MS) among men in the armed forces.

Aims—To document and explore possible explanations for the observed excess.

Methods—We analysed data on underlying cause of death and last full-time occupation for 3,688,916 deaths among men aged 20-74 years in England and Wales during 1979-2010, calculating proportional mortality ratios (PMRs) standardised for age. We compared PMRs for MS in the armed forces with those for each main social class, and in selected other occupations. We also compared PMRs for MS with those for motor neurone disease (MND).

Results—The overall PMR for MS in the armed forces during 1979-2010 was 243 (95%CI 203-288). The excess was apparent in each of three separate decades of study (PMRs, ranging from 220 to 259), and across the entire age range. PMRs for MS were not elevated to the same extent in comparator occupations, nor in any of the main social classes. There was no parallel increase in PMRs for MND.

Conclusions—These findings suggest that the high proportional mortality from MS in British military personnel is unlikely to have occurred by chance, or as an artefact of the method of investigation. However, the only military cohort study with published results on MS does not support an increased risk. It would be useful to analyse data on MS from other established military cohorts, to check for evidence of a hazard.

Keywords

Army; forces; military; mortality; multiple sclerosis

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Introduction

Multiple sclerosis (MS) is a chronic inflammatory disease of the central nervous system with a prevalence in the UK of approximately 200 per 100,000 (1). Its incidence peaks between 40 and 50 years of age, and typically it causes progressive disability over many years before eventually proving fatal in those who do not die first from other causes. In some cases, however, the course is more rapid. There is evidence that individuals can be genetically predisposed to the disorder, and that its development is influenced also by environmental factors such as vitamin D deficiency, smoking, Epstein-Barr virus infection, cytomegalovirus infection and circadian disruption (2,3). A striking epidemiological feature is its relationship to latitude, incidence being higher further from the equator, even within the same country (1,4).

We have previously published analyses of proportional mortality by occupation in England and Wales, based on records of last full-time occupation and cause of death obtained from death certificates (5–7). In the course of our most recent analysis (8), we noticed that proportional mortality ratios (PMRs) for MS in male members of the armed forces had been consistently elevated over three successive decades. There were several possible explanations for this finding, which might operate singly or in combination.

First, it could be an artefact of the study method. It is possible that men who develop MS during military service tend not to obtain civilian employment when they leave the armed forces, in which case their last full-time occupation will be recorded as military. In contrast, colleagues who die at the same age, but from diseases or injuries which do not cause a long preceding period of disability, may more often have obtained another job after leaving the forces, and therefore be registered with that more recent occupation. Selective re-employment of this type would spuriously increase the proportion of MS among deaths assigned to military occupations, especially at older ages. Any such bias might be expected to apply also to other occupations which workers commonly leave before normal retirement age (e.g. in the police and fire services and professional sport), and to extend to other chronically disabling diseases that affect young and middle aged adults (e.g. motor neurone disease (MND)).

Second, it could be that members of the armed forces have unusually low mortality from common causes of death such as cardiovascular and respiratory disease. If so, the proportion of deaths from MS would tend to be elevated, and a similar effect might be expected for many other diseases, including MND.

Another possibility was confounding by non-occupational factors related to lifestyle. Although in the most recent decade (2001-2010), members of the UK armed forces were variously assigned to higher managerial and professional, lower managerial and professional, and intermediate social classes, historically, it has not been possible to adjust their mortality for socioeconomic status because they were placed in a separate social class from all other occupations. If, however, their high PMR for MS were attributable to non-occupational factors determined by social background, one might expect to see similarly high PMRs in at least one of the main social classes.
Lastly, although there is no established hazard of MS in the military (9), the high PMRs could be a pointer to a previously unrecognised occupational cause of the disease.

To explore these possible explanations, we carried out a more detailed analysis of our dataset.

**Methods**

Data were supplied by the Office for National Statistics (ONS) (previously the Office of Population Censuses and Surveys (OPCS)), and covered all deaths among men aged 20-74 years in England and Wales during 1979-2010 (but excluding 1981 when records were incomplete). Information from death certificates on age at death, underlying cause of death, and last full-time occupation was used to derive PMRs with associated 95% confidence intervals (CIs) for combinations of occupation and cause of death (analysis being restricted to deaths with recorded occupations). Expected numbers of deaths were calculated with stratification by 5-year age band, taking all occupations combined as the standard. However, because as already explained, the military until recently were assigned to a separate social class from other occupations, we made no adjustment for social class.

For the purposes of this report we focused principally on deaths from MS (ICD9 340, ICD10 G35) in the armed forces. No distinction was possible between the separate armed forces or between ranks. We compared PMRs for MS in the military with those for each of the main social classes, and also with those of other occupations which like the military, have a relatively early retirement age (police, fire service and professional sportsmen). To check further the specificity of our findings, we derived similar statistics for MND (ICD9 335.2, ICD10 G12.2). Finally, we broke PMRs down by age band (20-44, 45-59, and 60-74 years) to check whether the elevation of proportional mortality was confined to older ages, at which, in the absence of disability, most former military personnel would have moved on to other jobs.

**Results**

During the 31-year period of study, there were 3,688,916 deaths among men aged 20-74 years with recorded occupations (1,564,981 during 1979-80 and 1982-1990; 1,199,234 during 1991-2000; and 924,701 during 2001-10). This included 26,507 deaths in men whose last occupation was recorded as military. A total of 7,485 deaths were from MS, including 129 in the armed forces, which gave an overall PMR of 243 (95%CI 203-288). As indicated in Table 1, the excess of deaths was consistent across the three decades that were studied, PMRs ranging from 220 (95%CI 161-293) to 259 (95% CI 180-360).

Table 1 also shows PMRs for MS in each of the main social classes. Proportional mortality was highest in social classes 1 and 3 non-manual, but even in these groups, PMRs were much lower than those for the armed forces. Among men in semi-skilled and unskilled manual occupations (the social background from which many non-officer military personnel in the UK are recruited (10)), PMRs for MS were all well below 100.
Table 2 compares PMRs for MS and MND across the full study period, in the armed forces, policemen, fire service and sportsmen. Among the military, the PMR for MND was significantly elevated, but much lower than that for MS (130 vs. 243). PMRs for both diseases were significantly high in policemen (168 and 150 respectively), but again, well below that for MS in the armed forces. In firemen, the PMR for MS was similar to that in policemen (153), while that for MND was close to expectation. Sportsmen had a significantly high PMR for MND (202), but a low PMR for MS.

Table 3 breaks down the analysis of mortality from MS and MND in the armed forces by age band, again aggregating data across the entire study period. The excess of deaths from MS was apparent in each age band, and the PMR at age 20–44 years (197, 95%CI 126-293) was only a little lower than at ages 60–74 years (238, 95%CI 180-308). Proportional mortality for MND was significantly elevated at ages 20–44 years, but at older ages was unremarkable.

Discussion

Men from the armed forces in England and Wales have experienced elevated proportional mortality from MS in each of three successive decades, with PMRs between 220 and 259 at ages 20-74 years. The consistency and statistical significance of the excess indicate that it is most unlikely to have occurred simply by chance. Moreover, our findings suggest that it cannot be explained entirely by selective exclusion from other employment when leaving the military, by low mortality in servicemen from the most common causes of death, or by non-occupational factors related to social class. The possibility of an unidentified occupational hazard remains.

Our data came entirely from death certificates, which are not always accurate. Errors may occur both in the assigned cause of death (11), and in the registered occupation. However, diagnostic errors are unlikely to have affected military personnel differentially, and therefore would not be expected to elevate PMRs from MS spuriously. Non-differential errors in diagnosis would tend to obscure a true hazard. Information about the last occupation of the deceased was provided by the person who registered the death and may also have been inaccurate (12). In particular, relatives sometimes report the main lifetime job rather than that held most recently, especially if the main job is viewed as more prestigious, as may be the case for the armed forces, police and fire service (13). However, in a PMR analysis, this would cause bias only if misreporting were more frequent for some causes of death than others, which seems unlikely.

Our finding that the PMR for MS in the military was elevated even at age 20–44 years, makes it less likely that the excess arose from selective failure to find civilian employment after leaving the armed forces. Moreover, there was no comparable increase in PMRs for MS in other occupations that workers commonly leave before normal retirement age. Also, PMRs in the military for MS were substantially higher than for MND, although it should be noted that the period of disability which precedes death from MND is usually shorter than for MS. Previous studies have suggested an increased risk of amyotrophic lateral sclerosis and MND in military occupations (14,15), which makes the higher PMR that we observed for MS even more remarkable.
Military service requires a higher level of fitness than most other occupations, which might tend to reduce mortality from common causes of death such as coronary heart disease and chronic respiratory disease. A recent study of all-cause mortality amongst UK armed forces personnel deployed to the 1982 Falklands Campaign suggests this may be the case, with Standardised Mortality Ratios lower than expected in every year from 1982-2012 when compared to the UK general population (16). Our own recent analysis also shows low PMRs for ischaemic heart disease in male members of the armed forces in each of the three successive decades. However, if the high PMRs that we observed for MS were attributable to this low mortality from the most common causes of death, then we would have expected to find similarly high PMRs for MND, which we did not.

Members of the armed forces come from a variety of social backgrounds, but the non-commissioned soldiers who make up the large majority, are predominantly from relatively poor circumstances (10). We found that PMRs for MS in semi-skilled and unskilled workers were below the average for all occupations, and even in social classes 1 and 3 non-manual, which had the highest proportional mortality, PMRs were well below those for the armed forces.

When viewed together, our findings suggest that the persistently high proportion of deaths from MS in British military personnel is unlikely to be explained by chance, bias or confounding. The alternative possibility that there is an underlying occupational hazard is plausible. For example, the close proximity in which military recruits live and work might facilitate the transmission of one or more infections that trigger later MS. However, before stronger conclusions can be drawn, there is a need to confirm the excess risk in cohort studies, which are less prone to bias than cross-sectional analyses of mortality such as ours.

We have been able to identify one such study from which findings on MS were reported in a PhD thesis (17). In that investigation, no increased incidence of hospital admission for MS was observed in former military personnel as compared with non-military controls, although the numbers were rather small. They did, however, have a higher incidence of admission for MND.

Given the suspicions raised by our analysis, we suggest that there is now a case for re-analysing data from other military cohorts that are already under follow-up, to check whether they give any support to the possibility of an occupational hazard.

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**References**

1. Mackenzie IS, Morant SV, Bloomfield GA, MacDonald TM, O’Riordan J. Incidence and prevalence of multiple sclerosis in the UK 1990-2010: a descriptive study in the General Practice Research Database. J Neurol Neurosurg Psychiatry. 2014; 85:76–84. [PubMed: 24052635]

2. O’Gorman C, Lucas R, Taylor B. Environmental risk factors for multiple sclerosis: a review with a focus on molecular mechanisms. Int J Mol Sci. 2012; 13:11718–11752. [PubMed: 23109880]
3. Dendrou CA, Fugger L, Friese MA. Immunopathology of multiple sclerosis. Nat Rev Immunol. 2015; 15:545–558. [PubMed: 26250739]

4. Simpson S Jr, Blizzard L, Otahal P, Van der Mei I, Taylor B. Latitude is significantly associated with the prevalence of multiple sclerosis: a meta-analysis. J Neurol Neurosurg Psychiatry. 2011; 82:1132–1141. [PubMed: 21478203]

5. Drever, F., editor. Occupational Health Decennial Supplement (Series DS no. 10). London: HMSO; 1995.

6. Coggon, D., Harris, EC., Brown, T., Rice, S., Palmer, KT. Occupational mortality in England and Wales 1991-2000. Office of National Statistics; 2009. http://www.ons.gov.uk/ons/rel/occupational-mortality/occupational-mortality-in-england-and-wales/occupational-mortality/occupational-mortality-in-england-and-wales--1991-2000.pdf

7. Coggon D, Harris EC, Brown T, Rice S, Palmer KT. Work-related mortality in England and Wales 1979-2000. Occup Environ Med. 2010; 67:816–822. [PubMed: 20573846]

8. Harris EC, Palmer KT, Cox V, Darnton A, Osman J, Coggon D. Trends in mortality from occupational hazards in England and Wales during 1979-2010. Occup Environ Med. 2016; 73:385–393. [PubMed: 26976946]

9. The Independent Medical Expert Group. Report and recommendations on medical and scientific aspects of the Armed Forces Compensation Scheme. UK: MOD; 2013 May 17. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/200140/imeg_report_2013_final.pdf

10. House of Commons Defence Committee, Duty of Care, (Third Report of Session 2004-05). Vol. 2. Analysis of socio-economic and educational background of non-officer recruits’. Memorandum to the House of Commons Defence Committee; 2004. p. Ev 255-257.

11. Swift B, West K. Death certification: an audit of practice entering the 21st century. J Clin Pathol. 2002; 55:275–279. [PubMed: 11919211]

12. Steenland K. Excess deaths due to occupation. Occup Environ Med. 2016; 73:497–498. [PubMed: 27317432]

13. Office of Population, Censuses and Surveys. Decennial supplement of occupational mortality 1970-1972 (Series DS 1). London: HMSO; 1978.

14. Weisskopf MG, O’Reilly EJ, McCullough ML., et al. Prospective study of military service and mortality from ALS. Neurology. 2005; 64:32–37. [PubMed: 15642900]

15. Bergman BP, Mackay DF, Pell JP. Motor neurone disease and military service: evidence from the Scottish Veterans Health Study. Occup Environ Med. 2015; 72:877–879. [PubMed: 26468494]

16. Ministry of Defence. A study of deaths among UK Armed Forces personnel deployed to the 1982 Falklands Campaign: 1982 to 2012. MOD; 2013. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/365217/Falkland-deaths-31_december_2012.pdf [3rd January 2017, date last accessed]

17. Bergman, BP. The Scottish veterans health study: a retrospective cohort study of 57,000 military veterans and 173,000 matched non-veterans. PhD thesis; University of Glasgow: 2015. http://theses.gla.ac.uk/7144/
### Key points

- The proportion of deaths from multiple sclerosis among men in the UK armed forces has been markedly and persistently elevated across three successive decades.

- This excess is unlikely to have occurred by chance or as an artefact of the method of analysis, but is inconsistent with findings from the only published cohort study that has addressed the risk of MS in military personnel.

- Analysis of data from other established military cohorts is needed to check for evidence of a hazard.
Table 1
Mortality from multiple sclerosis in armed forces and social classes by calendar period, men aged 20-74 years, 1979-80 and 1982-2010

| Job group/social class                      | 1979-80, 1982-90 | 1991-2000 | 2001-10 |
|--------------------------------------------|------------------|-----------|---------|
|                                            | All causes       | Multiple sclerosis | All causes       | Multiple sclerosis | All causes       | Multiple sclerosis |
|                                            | Deaths           | PMR (95% CI)      | Deaths           | PMR (95% CI)       | Deaths           | PMR (95% CI)       |
| All occupations                            | 1,564,981        | 2,819      | 2,199,234 | 2,088      | 924,701         | 2,578      |
| Armed forces                                | 10,037           | 48         | 255       | 35         | 259             | (180-360)  |
| Social class 1                              | 53,580           | 170        | 176       | 50         | 144             | 165        | (139-194)  |
| Social class 2                              | 283,189          | 591        | 116       | 235        | 479             | 117        | (107-128)  |
| Social class 3N                             | 164,324          | 449        | 152       | 111,880    | 304             | 156        | (139-175)  |
| Social class 3M                             | 556,721          | 905        | 90        | 429,686    | 713             | 95         | (88-103)   |
| Social class 4                              | 333,872          | 474        | 79        | 246,187    | 300             | 70         | (62-78)    |
| Social class 5                              | 163,258          | 182        | 62        | 117,513    | 113             | 55         | (46-66)    |
| Higher Managerial and Professional          |                 |            |           |            | 84,169         | 327        | 139        | (125-155)  |
| Lower Managerial and Professional           | 138,792          | 540        | 140       | (138-152)  |
| Intermediate                               | 53,018           | 260        | 176       | (155-199)  |
| Small employers and own account workers     | 137,992          | 298        | 77        | (69-87)    |
| Lower supervisory and technical             | 154,946          | 444        | 103       | (93-113)   |
| Semi-routine                               | 137,905          | 320        | 83        | (74-93)    |
| Routine                                    | 217,879          | 389        | 64        | (58-71)    |

PMR = proportional mortality ratio adjusted for age in five-year bands. 95% CI = 95% confidence interval
### Table 2
Mortality from multiple sclerosis and motor neurone disease in armed forces, police, fire service and sportsmen, men aged 20-74 years, 1979-80 and 1982-2010

| Job group       | Deaths from all causes | Multiple sclerosis | Motor neurone disease |
|-----------------|------------------------|--------------------|-----------------------|
|                 | Deaths | PMR (95%CI) | Deaths | PMR (95%CI) | Deaths | PMR (95%CI) |
| All occupations | 3,688,916 | 7,485 | 14,182 |          |          |          |
| Armed forces    | 26,507  | 129  | 243   | (203-288) | 131 | 130 | (109-155) |          |          |          |
| Police          | 21,511  | 81   | 168   | (133-208) | 133 | 150 | (126-178) |          |          |          |
| Fire service    | 7,368   | 25   | 153   | (99-226)  | 30  | 103 | (70-147)  |          |          |          |
| Sportsmen       | 2,174   | 3    | 57    | (12-166)  | 18  | 202 | (120-319) |          |          |          |

PMR = proportional mortality ratio adjusted for age in five-year bands and calendar period in three bands. 95%CI = 95% confidence interval
| Age band (years) | Deaths from all causes | Multiple sclerosis | Motor neurone disease |
|------------------|------------------------|--------------------|-----------------------|
|                  | Deaths | PMR (95% CI) | Deaths | PMR (95% CI) | Deaths | PMR (95% CI) |
| 20-44            | 3,616  | 24 (126-293) | 14     | 205 (112-343) |
| 45-59            | 4,128  | 48 (208-374) | 21     | 100 (62-153)  |
| 60-74            | 18,763 | 57 (180-308) | 96     | 132 (107-161) |

PMR = proportional mortality ratio adjusted for age in five-year bands and calendar period in three bands. 95%CI = 95% confidence interval.