Epidemiology of multiple sclerosis in US veterans
VIII. Long-term survival after onset of multiple sclerosis

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Summary
Survival to 1996 was analysed for nearly 2500 veterans of World War II who were rated as ‘service-connected’ for multiple sclerosis as of 1956 by the then Veterans Administration. Survival from onset was defined for all white women and black men, and a random sample of white men. Median survival times from onset were 43 years (white females), 30 years (black males) and 34 years (white males). Crude 50-year survival rates were 31.5% (white females), 21.5% (black males) and 16.6% (white males), but only the white females and white males were significantly different. A proportional hazard analysis was used to identify risk factors for mortality from multiple sclerosis onset year. Significant risk factors included male sex (risk ratio: 1.57), older age at onset (risk ratio: 1.05 per year) and high socioeconomic status (risk ratio: 1.05 per socioeconomic status category). There were no statistically significant differences in survival following multiple sclerosis onset by race or latitude of place of entry into military service, both significant risk factors associated with the development of multiple sclerosis. Standardized mortality ratios utilizing national US data (for 1956–96) showed a marked excess for all three race–sex groups of multiple sclerosis cases, with little difference among them, but with a decreasing excess over time. Relative survival rates, used to compare the survival of multiple sclerosis cases with that of other military veterans, did not differ significantly by sex–race group, nor by latitude of place of entry into military service, but did differ significantly by socioeconomic class. The lack of difference in male and female relative survival rates suggests that the significant difference in survival between male and female multiple sclerosis cases is, at least in part, a result of sex per se and not the disease.

Keywords: multiple sclerosis; survival; veterans

Abbreviations: EAD = entry into active duty; KC = Korean Conflict; SES = socioeconomic status; SMRs = standardized mortality ratios; VA = Department of Veterans Affairs (formerly Veterans Administration); WWII = World War II

Introduction
Multiple sclerosis is an inflammatory demyelinating disorder of the CNS that affects individuals in their most productive ages and is a tremendous burden for years to come. Defining the natural history of this disease will help in making rational treatment decisions and assist in unravelling its aetiology. In seven previous papers, we explored the epidemiology of multiple sclerosis using an unusually large cohort of multiple sclerosis cases and pre-illness matched controls comprising US veterans of World War II (WWII) and the Korean Conflict (KC) (Kurtzke et al., 1979, 1985, 1992; Norman et al., 1983; Page et al., 1993, 1995a; Kurtzke and Page, 1997). In this report, we examine the long-term survival experience following multiple sclerosis among WWII veterans.

The US veteran population is an exceptional resource for the study of disease. It comprises a very large population well indexed at many points of medical interest, and with the potential for long-term follow-up study that is unparalleled in the US. During WWII, 16 million young men and women served in the military, where medical care was available without regard to prior residence or socioeconomic status (SES). A diagnosis of multiple sclerosis made one ineligible for military service so that cases discovered in service were at or near clinical onset. Furthermore, whenever the diagnosis was entertained in the service, neurological evaluation was unusually thorough as the diagnosis was cause for medical discharge, which also made individuals eligible for service-connected disability care and compensation. After discharge from the military, veterans with service-connected disabilities were eligible for later medical care within the Department of Veterans Affairs health system, again without regard to prior residence or SES.

A number of studies have been published defining the
survival characteristics of multiple sclerosis patients (Bramwell, 1917; Brain, 1936; Ipsen, 1950; Carter et al., 1950; Lazarte, 1950; Leibowitz et al., 1969; Kurtzke et al., 1970; Visscher et al., 1984; Phadke et al., 1987; Riise et al., 1988; Poser et al., 1989; Wynn et al., 1990; Miller et al., 1992; Sadovnick et al., 1992; Brønnum-Hansen et al., 1994; Midgard et al., 1995; Kantarci et al., 1998). More recent cohorts have shown improved survival with mean survival figures of $>25$ years (Phadke et al., 1987; Riise et al., 1988; Poser et al., 1989; Kantarci et al., 1998). The question to be addressed in this report is whether the risk factors that influence the diagnosis of multiple sclerosis also play a significant role in survival subsequent to multiple sclerosis. Regarding such risk factors, we earlier reported that multiple sclerosis was most common in the northern tier states, intermediate in the middle tier and lowest in the southern tier (Kurtzke et al., 1979). White women had roughly twice the risk of multiple sclerosis as white men, with black men having half the risk of white men, regardless of geography (Kurtzke et al., 1979). Age at multiple sclerosis onset was found to be youngest in the northern tier states and oldest in the southern tier (Kurtzke et al., 1992). We also found striking correlations of population ancestry with multiple sclerosis risk, especially for Swedish/Scandinavian ancestry, even when controlling for the effects of latitude (Page et al., 1993, 1995a). In a multivariate analysis, latitude, years of education, urban versus rural address, high SES and poor visual acuity at induction were all significant risk factors for developing multiple sclerosis among white male WWII, black male WWII and white male KC veterans (Kurtzke and Page, 1997).

There has been disagreement between studies regarding risk factors for survival after multiple sclerosis. Variables that have differed include age at onset, sex, geographic latitude and onset symptoms. Thus, studies of the relationships between acknowledged multiple sclerosis risk factors and multiple sclerosis survival have produced uneven results. Here we examine the effects of such factors on survival subsequent to multiple sclerosis in US veterans.

**Patients and methods**

The entire series has been described in detail earlier (Kurtzke et al., 1979) and consists of 5305 US veterans of WWII or the KC who were judged by the Department of Veterans Affairs as ‘service-connected’ for multiple sclerosis. Such a decision for this disease required definitive evidence of clinical signs attributable to multiple sclerosis during or since ~1960 within 7 years after military service, and was made without regard to rank, race, sex or financial status. About half the cases were ascertained from the 1956 Veterans Affairs Medical Center (VA) roster of service-connected cases, when the presumptive period for service connection was 2 years after discharge. The remainder were ascertained from the 1969 VA roster, by which time the presumptive period had been extended to its (current) post-service interval of 7 years. In this report, only cases ascertained in 1956 were assessed in order to minimize the interval between onset and entry into the service. Each multiple sclerosis patient was matched to a military control using year of birth, date of entry into and branch of series, and survival of the war. A random sample of 80 cases was reviewed for diagnosis (J.F.K.), and 96% met all criteria of the Schumacher Panel for definite multiple sclerosis (Schumacher et al., 1965).

All materials were abstracted from the military records of the subjects.

Race and sex for each war cohort are represented here by three sex–race groups: white women, white men and black men. There were insufficient numbers of black women and subjects of other races to permit their study. Although data on entry into active duty (EAD) are available for all, data on other risk factors were not abstracted for all subjects because of financial strictures. We obtained such material for all women and all non-white cases. For white male subjects, risk factor data were gathered only for migrants (persons born in one geographic tier—north, middle or south, who entered military service in another) and for a 12.5% (i.e. 1 in 8) random sample of non-migrants (Kurtzke et al., 1979, 1985). Thus the sampling weight for white female, black male and white male migrants was one, and the sampling weight for white male non-migrants was eight. Latitude of residence at EAD was abstracted from the subjects’ military records, as was information to calculate the SES score. The SES score was based on occupation and education and coded according to the Bureau of the Census Standards (US Bureau of the Census, 1963). Age at onset was abstracted from either the military record or from VA compensation records. For graphing purposes, age at onset was categorized into two age groups: $\leq 25$ years and $\geq 26$ years.

Using these sampling weights yields a maximum effective sample of 2489, reduced because of missing data to 2038 when socioeconomic data were examined. Survival is shown for the first 50 years after onset. When analyses were based on sampled data (e.g. all the Cox proportional hazards analyses), weighted analyses were performed. In the few instances in which data were available for all subjects (e.g. analyses were limited to sex, race and EAD tier), unweighted analyses were performed; this is the case for relative survival rates by race and EAD tier and for standardized mortality ratios (SMRs) by race and sex.

Vital status was ascertained to June 1996 by using the VA’s Beneficiary Identification and Records Locator Subsystem. Mortality from all causes was used as the outcome measurement and not just death from multiple sclerosis. A recent study of death reporting in WWII twins indicates that the VA receives notice of death ~95% of the time (Page et al., 1995b). For veterans receiving compensation, as is the situation for these multiple sclerosis cases, it is likely that mortality reporting is virtually complete.

All analyses were performed using the Statistical Analysis System (SAS) computer software (SAS Institute, 1988). PROC PHREG was used to fit multivariable Cox proportional
hazards models to the survival data. This procedure does not require any assumptions about the particular shape of the survival distribution (e.g. exponential or Weibull), but does require an assumption that the ratio of the hazard functions for any two individuals is constant (i.e. their hazards are proportional); this latter assumption is subject to statistical testing. Most important for our analysis is the fact that Cox proportional hazard models can be used for univariate analyses of risk factors as well as multivariate analyses that yield estimates of risk factor effects adjusted simultaneously for the effects of all other risk factors in the model. Additionally, the Cox proportional hazards models allow for left truncation (i.e. staggered entry into the cohort), which is the case when every individual is followed from his or her year of onset.

The multiple sclerosis cases in this analysis were accessed from the VA compensation files, as of 1956. For the Cox regression analysis, however, we calculated survival from a more clinically meaningful base date, year of first symptom onset. To do this, we limited post-onset survival only to observed survival, which begins only when the case was actually accessed. This is accomplished by excluding all periods of unobserved survival from the analysis (e.g. if onset were in 1945 and accession in 1956, the period from 1945 to 1955). PROC PHREG permits such exclusions.

Given the suggestion by Sigrid Poser (Poser et al., 1989) that survival differences among subgroups of multiple sclerosis patients may actually reflect demographic differences, rather than disease processes, both relative survival rates and SMRs were calculated. Because of small samples in white females and black male groups, these relative survival rates were interpolated between years when either case or control rates were unchanged. SMRs provide a comparison of multiple sclerosis case mortality with the mortality of the entire US general population, rather than just military veterans. SMRs were calculated by using the software package OCMAP Plus (Marsh et al., 1998). The starting point was the base date of 1956 (case accession date) rather than onset date.

Results
Table 1 shows effective (i.e. weighted) sample sizes, and crude mortality rates by sex and race groups. Crude mortality rates are 68.5, 78.5 and 83.4%, respectively, for white females, black males and white males. The three crude rates are statistically different [$\chi^2(2) = 11.07, P = 0.004$], but the only statistically significant individual rates are for white females and white males [$\chi^2(1) = 10.68, P = 0.001$]; in particular, crude mortality rates for black males and white males are not statistically different [$\chi^2(1) = 1.345, P = 0.25$].

Figure 1 shows 50-year survival subsequent to multiple sclerosis onset for white females, white males and black males. Median survival times are ~43 years for white females, 30 years for black males and 34 years for white males. White female survival remains uniformly higher than both white male and black male survival, while white male and black male survival curves are much closer together, crossing twice in the 50-year interval. Thus, the survival distribution generally reflects the crude mortality rates. Figures 2–4 show similar data for each of the single factors age at onset, EAD tier and SES, respectively. Multiple sclerosis cases with older age at onset have lower survival rates throughout the 50-year period (Fig. 2), while survival rates by EAD tier (Fig. 3) do not appear to differ. Although survival rates by SES show some overlap (Fig. 4), multiple sclerosis cases with low SES do have a higher survival rate than cases with high SES throughout the entire 50-year follow-up. This trend was statistically significant.

Having examined the individual effects of various factors on multiple sclerosis survival, we then proceeded to a multifactorial analysis in which the effects of each independent factor are adjusted for all the others. The results of this analysis are shown in Table 2 as risk ratios. Age at onset (measured in years), sex and SES each had independent and significant effects on multiple sclerosis survival; neither race nor EAD tier had a significant effect. Removing race and EAD tier from the analysis resulted in a reduced model, also shown in Table 2. In the full model, each year of additional age at onset increases the risk of mortality by 1.07 (i.e. for 5 years, the increased risk is 1.38), males have a 1.8 higher mortality risk than females, and each additional higher SES class increases mortality risk by ~5%.

We then examined relative survival, which was calculated by dividing multiple sclerosis case survival rates by veteran control survival rates for subjects in the various sex, race, EAD and SES categories. A value of 1.00 indicates that multiple sclerosis cases and veteran controls have the same survival, while a value of 0.5, for example, would indicate that multiple sclerosis cases had exactly one-half the survival of veteran controls. Relative survival begins at 1.00 (i.e. cases and controls have equal survival) and declines more or less steadily as follow-up progresses. Figure 5 shows relative survival by sex and race group. Except at commencement of follow-up, multiple sclerosis cases always have poorer survival than their veteran counterparts. By 20 years after the accession date, white male case survival is only about two-thirds of that for white male veteran controls, while after 40 years, white male relative survival is closer to one-third. Although white females maintain a relative advantage in survival over white males for the entire time period, black male relative survival begins close to white male relative survival, dips below it and then exceeds it at

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**Table 1 Sample sizes and mortality statistics, by race and sex**

<table>
<thead>
<tr>
<th>Race–sex group</th>
<th>Number followed</th>
<th>Crude mortality in % (no. of deaths)</th>
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<tr>
<td>White female</td>
<td>92</td>
<td>68.5 (63)</td>
</tr>
<tr>
<td>Black male</td>
<td>79</td>
<td>78.5 (62)</td>
</tr>
<tr>
<td>White male</td>
<td>2318</td>
<td>83.4 (1934)</td>
</tr>
<tr>
<td>Totals</td>
<td>2489</td>
<td>82.7</td>
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~30 years. The meandering black male relative survival curve is in part due to small sample size. White male survival rates do not differ significantly by EAD tier (Fig. 6), but relative survival is uniformly higher among multiple sclerosis cases from the southern tier, compared with northern tier cases. Likewise, white male relative survival rates stratified by SES show a statistically significant divergence, with high SES doing worse for much of the follow-up, but are quite close together at the end of follow-up (Fig. 7).

SMRs have the advantage of using a very large control group, the US general population, but the disadvantage that the population rates are available for only broad demographic categories. Thus, for example, we can compare death rates for white male multiple sclerosis cases with rates for all US white males, but not all US veteran white males, or all high SES veteran white males. Figure 8 shows SMRs for multiple sclerosis cases by race and sex group. Except for black males in the last decade, SMRs for all race and sex groups are
>100 for the entire follow-up period of 40 years. There is an apparent tendency for SMRs to be greatest in the earlier follow-up years and to decline over time. In the final decade of follow-up, black male cases actually have better survival than black males of comparable age in the general population.

**Discussion**
Survival is a fundamental measure of disease severity. Ideally, it is best measured prospectively, from disease onset, and within a defined population. In the US, there have been two such population bases that have used this approach: Rochester, Minn. (Wynn et al., 1990) and the US armed forces (Kurtzke et al., 1970). A handful of other studies have utilized an incident cohort to study survival. Retrospective surveys, on the other hand, are hazardous and unreliable in the absence of some guarantee that incidence, and the sampling ratio, remain unchanged over the calendar period of estimation. For example, if the series is increasing in size, it will be biased toward early deaths.
Most studies published prior to the 1960s regarding the survival period after onset of multiple sclerosis reported time frames <17 years (Bramwell, 1917; Brain, 1936; Ipsen, 1950; Carter et al., 1950; Lazarte, 1950). These series were hospital-based with a bias towards the most severely affected patients. They were also performed during the pre-antibiotic era.

The original survival experience of the WWII Army hospital cohort showed a 25-year survival after onset of disease of 69% (Kurtzke et al., 1970). The survival curves were similar to those observed in a Mayo Clinic study (25-year survival 74%) (Percy et al., 1971) and the Lower Saxony study (25-year survival 63%) (Poser et al., 1989). The results of our study with median survival ranging between 30 and 43 years are in line with other recent incident cohorts with more recent onset of multiple sclerosis in the Danish (Bønnnum-Hansen et al., 1994) and Norwegian (Riise et al., 1988) studies but not in the Rochester study (Wynn et al., 1990). The interval between first symptom onset and diagnosis is ~4 years in Rochester (Wynn et al., 1990).

Our crude 40-year survival rates are lower than the nearly 40-year rates in the Danish multiple sclerosis population.

### Table 2

<table>
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<tr>
<th>Risk factor</th>
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<th>Risk ratio reduced model</th>
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<td>Age at 1956</td>
<td>0.993</td>
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<tr>
<td>Age at onset of multiple sclerosis (per year)</td>
<td>1.073*</td>
<td>1.067*</td>
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<tr>
<td>Sex (male versus female)</td>
<td>1.782*</td>
<td>1.779*</td>
</tr>
<tr>
<td>Race (black versus white)</td>
<td>0.965</td>
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<tr>
<td>EAD tier†</td>
<td>0.958</td>
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<tr>
<td>Socioeconomic status‡</td>
<td>1.048*</td>
<td>1.047*</td>
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*P < 0.001. †EAD is entry into active duty; risk is for each movement of a single tier northward (i.e. south to middle or middle to north within the continental US). ‡Per each higher socioeconomic class level (total of five).

Fig. 5 Relative survival by race and sex.
study (39% females and 25% males). The differences may be explained by better medical care and better access to medical care in Denmark, the higher proportion of females in the Danish cohort and a relatively high proportion of ‘possible multiple sclerosis’ cases (16.8%), if this last included other, less severe, neurological diseases. Three agents were approved for relapsing–remitting multiple sclerosis by the Federal Drug Administration between 1993 and 1996 [interferon-β 1b (1993), interferon-β 1a (1996) and glatiramer acetate (1996)]. It is unlikely that many veterans in the cohort were exposed to these immunomodulating medications. A lottery prevented wide access to interferon-β 1b when it was introduced initially in 1993, and the other two agents became available the year that follow-up was terminated.

Other multiple sclerosis survival studies have not, to our knowledge, addressed the variables of race or SES, both significant risk factors in developing multiple sclerosis. While black males tended to have significant survival risks somewhere between white males and white females in the actuarial
analysis, race was not a significant variable in the Cox regression analysis.

Comparison of the survival experience in our multiple sclerosis cohort was done with the US veteran population (utilizing relative survival) and the US general population (utilizing SMRs). Relative survival rates did not appear to differ by race or sex groups (Fig. 5). This was, in part, due to the small sample sizes for black males and white females which produced unstable estimates. Nonetheless, at 40 years post-multiple sclerosis onset, white male survival was less than that of both black males and white females. Examining relative survival by EAD tier in white males revealed no significant differences between rates, but there was a general trend for improved survival in the southern compared with the northern tier. The SMR data for all race–sex groups showed a gradual downward trend (Fig. 8). This trend reflects a higher risk for death in multiple sclerosis patients early on in the disease and a competing burden of death in the general population with time, thereby reducing the SMR. There were significant differences in relative survival by SES class among white males. Lower SES classes had a longer survival than higher SES classes. The major purpose for comparing our cohort with both the US and veteran controls was to contrast the unique survival experiences of both populations and also to allow us to compare our cohort with those from other studies.

Veteran survival is better than that of the US population as a whole. This has been described as the ‘healthy soldier effect’, denoting the fact that the military screens out applicants with health problems that would preclude them from performing rigorous physical duties. Nefzger calculated age standardized mortality ratios for WWII veterans between the years 1946 and 1965 (Nefzger, 1970). The observed mortality was 16% below expectation over the 20-year period. A more recent mortality study utilizing the Persian Gulf War veterans and other non-deployed veterans showed that both ratios are well below the mortality of the general US population, but the latter especially is of rather short duration. It has been postulated that the ‘healthy soldier effect’ ultimately disappears. The ‘healthy soldier effect’ probably has had a favourable effect on the survival experience of the current study cohort as compared with the general US population. Our total age-adjusted SMR was 2.18. This figure is similar to the total SMR figure of 2.0 from a large Canadian multiple sclerosis cohort (Sadovnick et al., 1992) and smaller than 3.25 (95% confidence interval: 3.11–3.38) from a large Danish multiple sclerosis cohort (Brønnum-Hansen et al., 1994). The causes of death in the current veteran cohort will be the subject of a future report.

Regarding risk factors for survival, we found that some of the factors which influence the development of multiple sclerosis have no significant influence on survival after multiple sclerosis. These factors include race and EAD tier. We did, however, find that female sex, lower SES and younger age at onset of multiple sclerosis significantly improved survival. Neither race nor EAD tier was significantly associated with survival after multiple sclerosis onset (Table 2).

As in the Israeli (Leibowitz et al., 1969), Danish (Brønnum-Hansen et al., 1994), Rochester (Wynn et al., 1990) and Lower Saxony (Poser et al., 1989) studies, we
saw higher survival in females and lower survival in later-onset cases. However, unlike the Norwegian (Riise et al., 1988; Midgard et al., 1995), and Western US (Visscher et al., 1984) studies, we found this significant difference in survival by sex even after adjusting for other covariates, in particular age at onset. In addition, unlike the Western US (Visscher et al., 1984) study, we found no significant effect of latitude on survival. One could argue that there is a clinically significant improved survival for multiple sclerosis patients in the southern EAD tier based on the relative survival curves, despite the fact that EAD tier was not a significant predictor of survival in the reduced model. Alternatively, small numbers of non-white multiple sclerosis subjects and, therefore, limited power may be an explanation for this lack of significance. One interpretation of the SES data is that high SES is a precipitant of disease and for severity. This would suggest a subclinical state, which can be worsened to produce disease, and worsened further to result in death by some correlate of high SES. However, sex, race and geography do not support this interpretation.

Table 3 lists multiple sclerosis cohort studies that have reported risk factors for survival. The studies of Kurtzke, Riise, Poser, Wynn, Sadovnick, Brønnum-Hansen and Midgard were prospective in nature and involved incident cases. Other studies were based on prevalence surveys. The studies listed had different diagnostic criteria for multiple sclerosis, variable sample sizes and variable lengths of follow-up. Risk factors that tended to be in agreement across studies included age at onset of multiple sclerosis, with virtually all studies reporting that later age of onset of multiple sclerosis was associated with shorter survival compared with earlier onset. The exception to this was the study by Kurtzke showing a non-significant effect of age at onset on surviving the first 20 years of the follow-up. This finding is largely related to the young age of the cohort, with 58% of cases having onset between ages 20 and 29 years. Other risk factors that were in agreement across studies and predicted worse survival included: high initial disability scores, and progressive disease course.

In summary, our study showed that life expectancy in veterans with multiple sclerosis is significantly reduced compared with the US general population, but the difference lessens over time. Survival compared with veterans continued to worsen with follow-up time. Female sex, low SES and younger age at onset significantly improved survival in this cohort. Future studies hopefully will better clarify the

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<th>Country</th>
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ON = optic neuritis; NS = not significant.
relationships between race, sex, SES, ethnic background and survival in multiple sclerosis.

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References


Visscher BR, Liu K-S, Clark VA, Detels R, Malmgren RM, Dudley JP.

