SPECIAL ARTICLE

DELAYED EFFECTS OF THE MILITARY DRAFT ON MORTALITY

A Randomized Natural Experiment

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Abstract To study the effect of military service during the Vietnam era on subsequent mortality, we analyzed a randomized natural experiment, the military draft lottery of 1970 to 1972. Between 1974 and 1983, there were 14,145 deaths among California and Pennsylvania men whose dates of birth were in the years for which the draft lottery was held. The group of men with birth dates that made them eligible for the draft had a higher mortality rate than the group with birth dates that exempted them from the draft: suicide was increased by 13 percent ($P = 0.005$ by two-tailed test), death from motor-vehicle accidents by 8 percent ($P = 0.03$), and total mortality by 4 percent ($P = 0.03$).

Only 26 percent of the men who were eligible for the draft actually entered the military. If military service (rather than draft eligibility) was the actual risk factor, suicide and death from motor-vehicle accidents would have to have been increased by 86 percent and 53 percent among men who served in the military, to produce the increased risk that we observed among all draft-eligible men. A separate analysis that compared the causes of death in veterans and nonveterans yielded similar estimates: veterans were 65 percent and 49 percent more likely to die from suicide and motor-vehicle accidents, respectively. We conclude that the most likely explanation for these findings is that military service during the Vietnam War caused an increase in subsequent deaths from suicide and motor-vehicle accidents. (N Engl J Med 1986; 314:620-4.)

FOUR million Americans served in Indochina during the Vietnam War, and 800,000 were assigned to combat.[1] Higher rates of drug and alcohol abuse,[2,3] depression,[2,4] marital problems,[2,4] aggressive behavior,[5] arrests and convictions on criminal charges,[3] and "post-traumatic stress disorder"[1,3,6] have been found in this group of men after their return to civilian life. Recently, the controversy over Agent Orange has led to the first studies of delayed effects on mortality among Vietnam veterans.[7-9]

Comparisons between veterans and nonveterans may be biased because men who enter the military differ in important ways from men who do not. For example, men of low socioeconomic status, among whom mortality tends to be higher, may be less adept at avoiding military service. This factor would lead to an apparent excess of mortality among veterans. Selection bias can also act in the opposite direction because men with known medical problems are excluded from the military.[10]

We avoided selection bias by studying men involved in the draft lottery of 1970 to 1972. During those three years, 20-year-old men were randomly divided by the lottery into two cohorts: one that was eligible for the draft and one that was exempt. This study compares deaths during the decade after military service in these two cohorts by means of an "intention-to-draft" analysis that yields the same strength of causal inference as a randomized clinical trial.

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METHODS

Randomized Study

From computerized death-certificate registries of California and Pennsylvania, we obtained the date of birth and the cause of death for 14,145 men who were born in the United States in the period 1950 to 1952 and who died at least three years after their eligibility for the draft was established (Fig. 1). The cause of death was based on the *International Classification of Diseases* (ICD) code listed on the death certificate (ICD-8 [eighth revision] for deaths through 1978 and ICD-9 thereafter). "Suicide" was defined as ICD 950.0 to 959.9; "suicide by firearms" as 955.0 to 955.9; "motor-vehicle accident" as 810.0 to 823.9 in ICD-8 and 810.0 to 825.9 in ICD-9; "other accidents" as 800.0 to 809.9 and 824.0 to 949.9 in ICD-8 and 800.0 to 809.9 and 826.0 to 949.9 in ICD-9 (except for narcotic overdose); "homicide" as 960.0 to 969.9; "cancer" as 140.0 to 209.9; "cardiovascular disease" as 390.0 to 459.9; "cirrhosis of the liver" as 571.0 to 571.9; and "narcotic overdose" as 853.0 in ICD-8 and 850.0 in ICD-9. Men born outside the United States (11.8 percent of total deaths) were excluded when this information was available (87.5 percent of the deaths), because most would not have been eligible for the draft.

Draft eligibility was determined from tables provided by the U.S. Selective Service Commission. The dates of birth of "draft-eligible" men had lottery numbers that were below or equal to the highest lottery number drafted in each year (195 for men born in 1950, 125 for those born in 1951, and 95 for those born in 1952). "Draft-exempt" men had dates of birth with lottery numbers above the cutoff figure. The expected ratio of deaths between draft-eligible and draft-exempt men was based on the cutoff number for draft eligibility in each year. Because men born earlier were both more likely to be eligible for the draft (because of the changes in the cutoff figure) and more likely to die (because the follow-up period was longer), deaths were stratified according to year of birth. Combined relative risks, P values, and 95 percent confidence intervals were calculated with the Mantel–Haenszel method.[11] "Expected" deaths in draft-eligible men were the observed deaths divided by the relative risk — that is, the number of deaths that, if observed, would have given a relative risk of 1.

Of the 5,200,000 men in the United States who had been born in 1950 to 1952,[12] 4142 died in the Vietnam War.[13] Adjusting for these deaths and for slight monthly fluctuations in birth rate[14] did not change the results of our analysis.

Projection of Relative Risk from Military Service

We estimated the proportions of draft-eligible and draft-exempt men who entered the military within two years after draft eligibility had been determined, by using three sources of information: dates of birth of a random sample of 3000 men who entered military service in 1971 to 1973 (provided by the Defense Manpower Data Center), the number of entrants into the military each year (provided by the Selective Service Commission), and the number of men who were born in the United States in each year of birth studied (provided by the U.S. Census Bureau).[12] Projected relative risks from military service were computed with the assumption that the mortality rates observed in draft-eligible and draft-exempt men represented weighted averages of mortality rates in men who entered the military at the age of draft eligibility and in men who did not. Thus,

$$R_{\text{eligible}} = p_1A + (1-p_1)B \qquad (1)$$

and

$$R_{\text{exempt}} = p_2A + (1-p_2)B \qquad (2),$$

where A is the death rate among men who entered the military, B is the death rate among men who did not enter the military, p_1 is the proportion of draft-eligible men who entered the military, p_2 is the proportion of draft-exempt men who entered the military, R_{eligible} is the death rate in draft-eligible men, and R_{exempt} is the death rate in draft-exempt men. Equations 1 and 2 can be combined and rearranged to yield:

$$\frac{A}{B} = 1 + \frac{\dfrac{R_{\text{eligible}}}{R_{\text{exempt}}} - 1}{p_1 - p_2\dfrac{R_{\text{eligible}}}{R_{\text{exempt}}}} \qquad (3),$$

where A/B is the relative risk from military service and $R_{\text{eligible}}/R_{\text{exempt}}$ is the relative risk from draft-eligibility status.

Table 1. Observed and Expected Numbers of Deaths and Relative Risks of Death among Men Eligible for the Draft.*

Cause of Death	No. of Deaths (All Men Studied)	Deaths among Draft-Eligible Men		
		No. observed/ no. expected	Relative risk†	95% confidence interval
Suicide	2,356	966/856	1.13‡	(1.04–1.23)
By firearms	1,210	502/437	1.15§	(1.02–1.29)
By other means	1,146	464/419	1.11	(0.98–1.25)
Motor-vehicle accident	3,399	1,370/1,265	1.08§	(1.01–1.16)
All other causes	8,390	3,258/3,269	1.00	(0.95–1.04)
Other accidents	2,227	879/851	1.04	(0.95–1.13)
Homicide	1,972	760/771	0.99	(0.90–1.08)
Cancer	881	323/359	0.90	(0.79–1.05)
Cardiovascular disease	770	296/305	0.97	(0.83–1.13)
Cirrhosis of the liver	292	100/133	0.75§	(0.58–0.97)
Narcotic overdose	227	99/92	1.08	(0.82–1.40)
Other illness	2,021	801/760	1.05	(0.96–1.16)
All causes	14,145	5,594/5,389	1.04§	(1.00–1.08)

*This table presents counts rather than rates because only the numerators are known with precision. Relative risks are unaffected by the denominator, which cancels in the calculations. Based on approximate denominators from the census,[16] the age-adjusted death rates per 100,000 man-years of follow-up for total mortality, suicide, and motor-vehicle accidents were 193.7, 33.5, and 47.4, respectively, among draft-eligible men and 186.6, 29.6, and 43.8, respectively, among draft-exempt men.

†As compared with draft-exempt men.

‡P<0.01 by two-tailed test.

§P<0.05 by two-tailed test.

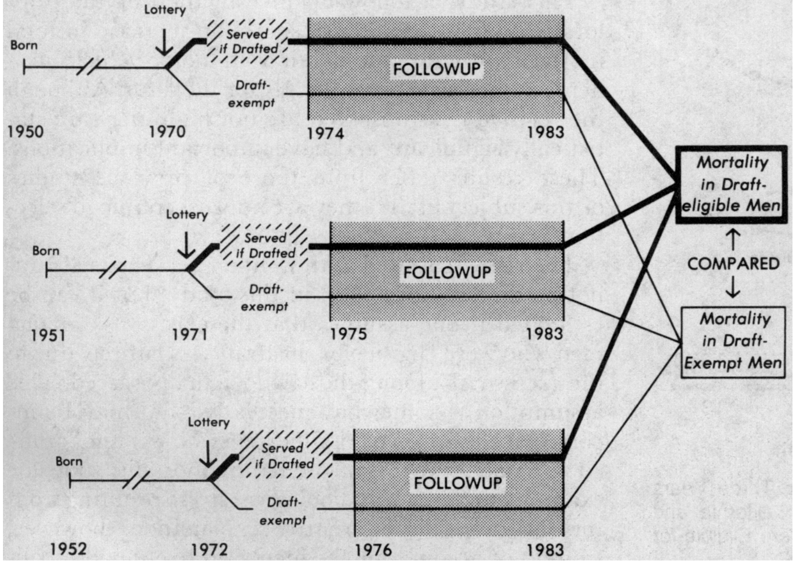

Figure 1. Design of a Randomized Study of Mortality among Men Who Were Eligible and Exempt from the Draft.

Case–Control Study

In 1979, the Pennsylvania death certificates registry began to include veteran status, which was available for 2003 (95 percent) of the 2105 deaths of subjects in this study in 1979 to 1983. In a separate analysis of these deaths, veteran status as a risk factor was compared in deaths from suicide, motor-vehicle accidents, or cirrhosis of the liver (cases) with deaths from all other causes (controls). Odds ratios, P values, and 95 percent confidence intervals were computed with standard methods.[15]

Results

Risk of Death Associated with Draft Eligibility

The relative risks of death among draft-eligible men, as compared with draft-exempt men, are shown in Table 1. Total deaths among draft-eligible men were 4 percent higher than expected (P = 0.03 by two-tailed test). The excess mortality was entirely due to excess deaths from suicide (13 percent excess; P = 0.005) and motor-vehicle accidents (8 percent excess; P = 0.03). The relative risks for most other causes of death were not significantly different from 1. The number of deaths from cirrhosis of the liver was significantly lower than expected (P = 0.03).

Table 2 shows the results according to state and race. The relative risks of death from suicide and motor-vehicle accidents were similar in both states. The relative risk for death from motor-vehicle accidents was higher among nonwhites, but the 95 percent confidence intervals overlapped.

Table 2. Relative Risk of Death among Draft-Eligible Men According to State and Race.*

CAUSE OF DEATH	RELATIVE RISK FOR DRAFT-ELIGIBLE MEN†				
		STATE		RACE‡	
	OVERALL (14,145)	CALIF. (10,272)	PENN. (3,873)	WHITE (11,533)	NONWHITE (2,448)
Suicide	1.13§	1.12¶	1.16	1.13§	1.09
Motor-vehicle accident	1.08¶	1.10¶	1.05	1.07	1.33¶
All other causes	1.00	1.02	0.94	1.00	0.98
All causes	1.04¶	1.05¶	1.00	1.04¶	1.02

*Numbers in parentheses are total numbers of deaths in each category of men included in the study.

†As compared with draft-exempt men.

‡Information on race was unavailable for 164 deaths. Of the nonwhite subjects, 93 percent were black.

§P<0.01 by two-tailed test.

¶P<0.05 by two-tailed test.

Secular Trends and Cohort Analysis

Figure 2 shows cumulative excess deaths among draft-eligible men. If excess mortality were confined to the first few years after draft eligibility, the curve would rise and then plateau. Although this may be true for deaths from motor-vehicle accidents, higher mortality from suicide appears to persist to the present, 13 years after the draft.

For men born in 1950, 1951, or 1952, the relative risks for total mortality were 1.048, 1.033, and 1.031, respectively. This difference was not statistically significant.

Estimated Effect of Military Service on Subsequent Mortality

The results above give relative risks associated with eligibility for the draft. These values can be converted to relative risks associated with military service by means of equation 3. Approximately 25.6 percent of draft-eligible men entered the military, as compared with 9.3 percent of draft-exempt men, who entered as volunteers. Table 3 shows projected relative risks for military service.

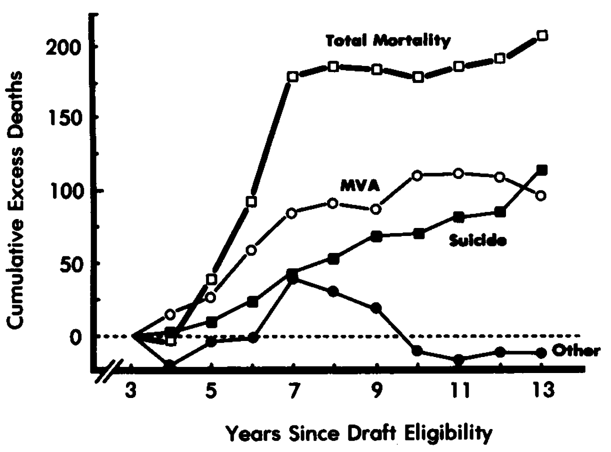

Figure 2. Cumulative Excess Deaths, Beginning Three Years after Determination of Draft Eligibility, among California and Pennsylvania Men Born in 1950 to 1952 Who Were Eligible for the Draft.

MVA denotes motor-vehicle accident.

Case–Control Study

We also determined the odds ratio for death by suicide, motor-vehicle accidents, and cirrhosis in veterans as compared with nonveterans among the 2003 Pennsylvania deaths for which veteran status was known (Table 4). This comparison, although subject to the selection biases discussed earlier, is a separate and nearly independent approach to estimating the increased risk of suicide and death from motor-vehicle accidents that is associated with military service. The results were similar to projections based on the draft lottery. The estimated increases in suicide and death from motor-vehicle accidents were 65 percent and 49 percent (Table 4), as compared with 86 percent and 53 percent (Table 3).

Table 3. Relative Risk of Death Observed among Men Eligible for the Draft and Projected among Those Who Actually Served in the Military.*

CAUSE OF DEATH	RELATIVE RISK	
	OBSERVED FOR ELIGIBLE MEN	PROJECTED FOR MEN WHO SERVED
Suicide	1.13	1.86
Motor-vehicle accident	1.08	1.53
All causes	1.04	1.25

*Projections assume that 25.6 percent of draft-eligible men and 9.3 percent of draft-exempt men served in the military and that all excess mortality among eligible men was due to excess mortality among those who served.

Discussion

This study, a follow-up investigation of the draft lottery of the early 1970s, shows an increase in total mortality, suicide, and death from motor-vehicle accidents in men who were eligible for the draft. Although the relative risks observed are not high, they are statistically significant and have important implications. These results differ from those of previous studies of this subject in that they are not susceptible to selection bias.

The risk associated with military service itself cannot be directly measured in this study, but it can be estimated if one assumes that the excess risk among men who were eligible for the draft was entirely due to the excess risk among those who actually served. This assumption is somewhat speculative and may be incorrect if the group of eligible men who were not drafted also had an excess of premature mortality, due, for example, to guilt or psychological stress resulting from the lottery. This alternative explanation, however, would not account for the increased likelihood of suicide and death from motor-vehicle accidents among

Table 4. Case–Control Analysis of Veteran Status as a Risk Factor for Death by Suicide, Motor-Vehicle Accident, and Cirrhosis of the Liver.*

Cause of Death	Number of Deaths		Odds Ratio	95% Confidence Interval	P Value
	Veteran	Non-veteran			
Suicide	107	218	1.65	(1.26–2.15)	0.0003
Motor-vehicle accident	133	300	1.49	(1.17–1.90)	0.002
Cirrhosis	10	32	1.05	(0.52–2.13)	>0.5
Other causes	276	927	—	—	—

*Based on data for 2003 men who were born in the United States from 1950 to 1952, who died in Pennsylvania between 1979 and 1983, and for whom veteran status was known. The analysis of suicide considers suicides as cases and other causes (except motor-vehicle accidents and cirrhosis) as controls; the analyses for motor-vehicle accidents and cirrhosis are analogous.

veterans in our case–control study and in previous nonrandomized studies.

A recent study of death certificates from New York, which used methods similar to those in our case–control study, showed statistically significant odds ratios of 1.62 for suicide and 1.76 for death from motor-vehicle accidents.[8] A similar study from Massachusetts showed odds ratios for Vietnam veterans of 1.46 for suicide and 1.50 for death from motor-vehicle accidents.[9] An Australian study also found higher rates of suicide and death from motor-vehicle accidents among Vietnam veterans, but the differences were not statistically significant.[7]

It is possible that the increased relative risk observed in California and Pennsylvania was offset by a decreased relative risk in the rest of the country. This could have occurred if draft-eligible men who were at high risk of suicide and motor-vehicle accidents were more likely than comparable draft-exempt men to move to California or Pennsylvania. This seems unlikely in view of the findings from other places discussed above and because our results were similar in California, which has net in-migration, and Pennsylvania, which has net out-migration.[17]

This study cannot determine the mechanism by which the draft may have had a delayed effect on mortality. Physical handicaps acquired during military service may have contributed to increased suicide and death from motor-vehicle accidents. Social and economic difficulties after the return to civilian life, increased susceptibility to mental illness, and greater familiarity with firearms may affect suicide rates. Factors that may contribute to increased deaths from motor-vehicle accidents include driving while intoxicated, suicidal driving, and changes in driving habits caused by psychological problems.[18]

The lower rate of death from cirrhosis among draft-eligible men is more difficult to explain; previous studies have indicated that problems with alcohol abuse are more common among veterans than nonveterans.[2,3] This lower risk was not confirmed in our case–control study (odds ratio, 1.05), in the New York study (odds ratio, 1.12), or in the Massachusetts study (odds ratio, 0.94). Although the lower rate of death from cirrhosis deserves further investigation, the most likely explanation is that this finding was due to chance.

The elevated risk among draft-eligible men, though small, is important because it applies to a very large population of men. If California and Pennsylvania are typical of the country, the 205 excess deaths we observed represent 1250 excess deaths nationally among men eligible for the draft in the period 1970 to 1972.[16] If the draft affected men similarly before the lottery system began, the earlier years of the draft may have caused thousands of additional premature deaths.

Increased mortality may represent only a fraction of the adverse sequelae of the draft, if nonfatal outcomes are also increased. Our methods could also be used to examine this possibility in an analysis of the birth dates of men with depression, injuries from motor-vehicle accidents, alcoholism, criminal convictions, divorce, or unemployment. However, the method will not be helpful in evaluating the possible toxic effects of Agent Orange, which was no longer used in Vietnam after mid-1970.[19]

This study has two important implications for prevention. It identifies a large group of men with an increased risk of premature death, which may be partly preventable. Even more important, it indicates that before sending young men to war, especially one in which they may have experiences similar to those of Vietnam veterans, those who make the decision should weigh all the costs. The casualties of forced military service may not be limited to those that are counted on the battlefield.

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MEDICAL INTELLIGENCE

IBUPROFEN-ASSOCIATED PURE WHITE-CELL APLASIA

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Ibuprofen is a nonsteroidal, antiinflammatory agent that is commonly used in the treatment of patients with rheumatoid arthritis[1] and osteoarthritis.[2] Although ibuprofen has a favorable therapeutic risk–benefit ratio,[3] a number of potentially serious adverse reactions have been associated with the use of this drug.[4,5] We investigated the mechanism of ibuprofen-induced reversible agranulocytosis and bone marrow granulocytic aplasia (pure white-cell aplasia) in a patient with osteoarthritis who had been receiving ibuprofen. We observed a circulating complement-dependent antibody that, in the presence of ibuprofen, profoundly inhibited the growth of autologous and heterologous myeloid progenitors in vitro.

Case Report

An 80-year-old man with osteoarthritis who was taking oral ibuprofen (600 mg twice a day) and who had no previous history of hematologic problems was found to have a white-cell count of 300 per cubic millimeter (100 percent lymphocytes), a normocellular marrow with almost no granulocytic precursors, striking plasmacytosis (23 percent), and no antineutrophil antibodies. The physical examination was normal. Other studies were notable only for an elevated rheumatoid factor (1:2560). The ibuprofen was discontinued and the patient recovered completely; two months later, the bone marrow was normal.

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Methods

Mononuclear cells that were isolated from the patient's bone marrow (at presentation and seven weeks after recovery) and from the bone marrow of a consenting normal adult volunteer were cultured (1 to 4×10^5 cells per milliliter) for erythroid progenitors (colony-forming units — erythroid and burst-forming units — erythroid) (in plasma clots), myeloid progenitors (colony-forming units — granulocyte/macrophage) (in agar), and pluripotent progenitors (colony-forming units giving rise to mixed colonies with granulocytic, erythroid, monocyte-macrophage, and megakaryocyte elements) (in methylcellulose) in the presence or absence of ibuprofen (0.1 to 25 μg per milliliter) with serum or IgG from the patient or the normal volunteer[6] (serum, 0.05 to 0.1 ml; IgG, 0.5 to 1.0 mg per milliliter) or with rabbit complement (Pel-Freeze Biologicals, Rogers, Ark.) (or with both), as previously described.[7]

Results

Despite the presence of severe neutropenia, the mean number of myeloid progenitors in the patient's marrow (±SEM) was near the normal value (26±2 colonies per 10^5 cells; normal, 34±10). Table 1 shows that the addition of different concentrations of the patient's serum to autologous marrow did not significantly inhibit the growth of myeloid progenitors in vitro. Similarly, complement or ibuprofen alone did not affect myeloid-progenitor activity. Moreover, the presence of any two of these agents also had no effect. In contrast, the simultaneous addition of the patient's serum, ibuprofen, and complement to the patient's marrow caused profound suppression of the growth of myeloid progenitors. No such inhibition was seen with normal serum (Table 1).

The results presented in Table 2 show that the inhibitory effect of the patient's serum on the growth of myeloid progenitors in marrow taken from the patient after recovery was attributable to the IgG fraction. This suppressive effect was also demonstrated in normal human bone marrow in vitro (Table 2). The effect of the patient's serum was restricted to myeloid progenitors; the growth of erythroid progenitors in marrow taken from the patient after recovery was not inhibited (79±11 vs. 69±4 per 10^5 cells). However, the development of pluripotent progenitors was suppressed in vitro in the presence of the patient's serum, ibuprofen, and complement (8.7±0.6 vs. 3.2±0.6 colonies per 10^5 cells).

Discussion

We have described the presence of a complement-dependent IgG antibody in a patient with reversible