MORBIDITY AND MORTALITY ASSOCIATED WITH EXPOSURE TO OTTO FUEL II IN THE U. S. NAVY 1966-1979

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SUMMARY

Problem

Over the past two decades the Navy's unique liquid propellant Otto Fuel II (OF II) has been used in the preparation and maintenance of MK 46 and MK 48 torpedoes. A variety of adverse health effects have been attributed to the analogous compounds nitroglycerine and ethylene glycol dinitrate and it is suggested that workers exposed to OF II may also experience these effects. In order to obtain a better understanding of the epidemiology of this potential disease-exposure relationship it is necessary to examine specific clinically apparent health outcomes in Navy personnel exposed to OF II.

Objective

The objective of this study was to assess whether the morbidity and mortality previously associated with analogous (nitrated ester) compounds would be found in Torpedoman's Mates (TM) potentially exposed to OF II.

Approach

This investigation was divided into two major parts. In the initial analysis, illness and/or death in sixteen cardiovascular, neurologic, and toxic diagnoses was compared among TMs potentially exposed to OF II (and appropriate control groups) during the fourteen-year period, 1966-1979. The second analysis focused the inquiry on selected cardiovascular diseases (acute myocardial infarction, angina, and cardiac arrythmias) that historically have been strongly associated with nitrated ester exposures. The second analysis covered the ten-year period 1970-1979. Inpatient medical files were used to ascertain the first appearance of any of the diagnoses on hospitalization, Medical Board, Physical Evaluation Board, or death records during this period. Hospitalization rates and appropriate confidence intervals were calculated and survival tables were used to calculate the probability of hospitalization. Estimates of age and occupation group-specific relative risks (odds ratios), were made to determine if there were any significant health risk differences between the study groups.

Results

Cardiovascular System (CVS) related hospitalization rates were consistently higher for TMs compared to PTs from 1973 through the end of the study interval. Although the temporal trends tended to parallel each other, the differences were not significant. There were also no significant age-specific hospitalization rate differences across the occupational groups.

While the initial investigation did not find statistically significant excess CVS morbidity and mortality in potentially OF II exposed TMs, the more refined second analysis suggested that potentially OF II exposed TMs had a significantly greater risk of being hospitalized with a CVS disease compared to other TMs and PTs during the 10-year study interval.

Conclusions/Recommendations

Elevated odds ratios observed for TMs (especially those TMs who worked with OF II) compared to PTs suggests that TMs work in an environment which places them at an increased risk for selected CVS disease outcomes. Appropriate workplace monitoring and medical surveillance of TMs to detect early symptoms of CVS disease is recommended.

INTRODUCTION

The U. S. Navy maintains a strong program designed to control occupational illness, disease, and injury in both its active duty and civilian workforces. The identification of health hazards and their associated risk of causing adverse outcomes are important aspects of the overall Navy Occupational Safety and Health (NAVOSH) program efforts (1).

Many workplace toxic hazards are common to both private industry and the military, a situation which allows the Navy to apply generally available scientific information. Some hazards, however, are Navy unique. In these instances activities covering a spectrum from research epidemiologic risk inquiries to development of specific health protecting strategies are best performed within the Navy community.

OF II is a Navy unique compound used increasingly in the last two decades. A variety of adverse health effects have been attributed to the analogous compounds nitroglycerin and ethylene glygol dinitrate.

This study was undertaken to assess whether excess morbidity and mortality, previously associated with analogous nitrated ester compounds, would be found in Navy occupational groups potentially exposed to OF II. Interest centered on clinically apparent health outcomes that would result in hospitalization, death or administrative action.

BACKGROUND

Otto Fuel II is a liquid propellant currently used in the preparation and maintenance of MK 46 and MK 48 torpedoes. It is a red-orange, free-flowing liquid with a distinctive odor. Chemically it is an aliphatic (alkyl) nitrate to which a desensitizing agent (2-nitro diphenylamine) and a stabilizer (di-n-butylsebacate) have been added. The physiologically active component of OF II is the nitrated ester, known as 1, 2-propylene glycol dinitrate (PGDN). PGDN is the component of OF II which is of medical concern. As with other widely used nitrated esters, nitroglycerin (NG) and ethylene glycol dinitrate (EGDN), it is known for its ability to produce vasodilation, headaches, dizziness, nausea, hypotension, and nasal congestion (2-5). PGDN appears to exhibit the same toxicological effects as EGDN and NG (6).

The suggestion that NG might be an occupational health hazard first appeared in the U. S. medical literature in the 1890s when Darlington (7) reported complaints of headaches, nausea, and dizziness in miners and tunnel workers who handled dynamite and inhaled both unexploded NG vapors and its explosion byproducts.

Laws (8) described the symptoms of NG exposure among dynamite makers and their wives, who laundered and ironed their clothes, underwear and bedclothes. A severe headache was the most prominent symptom. Other reports describing occupational exposures to NG and EGDN in workers in the explosives and pharmaceutical industries have confirmed the clinical effects first noted in the 19th century (9-12).

The most important signs and symptoms associated with initial exposure to nitrated esters are decreases in diastolic, systolic and pulse pressures, with diastolic pressures generally decreasing less than systolic or pulse pressures (10). These signs of initial exposure are indicative of a rapid and substantial shift in blood volume from the central to the peripheral circulatory

system initiated by dilation of the blood vessels (10). Most workers develop a tolerance to the vasodilation effects after the first few days and do not experience symptoms with repeated daily exposure (9). The development of tolerance is probably related to a compensatory vasoconstriction. Withdrawal from long-term exposure to NG or NG:EGDN mixtures has been associated with angina pectoris and sudden death in workers, particularly after weekends or holidays (13). It has been postulated that the compensatory vasoconstriction, which continues in the absence of exposure to the vasodilating agent, leads to spasms of the coronary arteries and these spasms are related to the angina and sudden death.

Although there are very few reports on the chronic effects of nitrated esters, recent studies by Hogstedt (14-15) reviewed death certificates (for 1955-1975) of two cohorts of workers from a county in Sweden in which there was a dynamite plant. Dynamite workers were more likely to die from heart disease than were other men in the same county. These epidemiological studies were noteworthy because they suggested that NG and EGDN not only may cause (in the 72-hour period after exposure ceases) coronary spasm, myocardial infarction and fatal arrhythmia, but also probably cause excess deaths from heart disease months and years after exposure ends. Prior to the aforementioned studies, previous studies (13,16,17) described the angina, coronary spasm, myocardial infarction, and sudden death only shortly after exposure had ceased. Thus, the Swedish studies raise the possibility that the mechanism of the cardiac toxic effects of NG and EGDN may be more complex than simply the precipitating of coronary spasm after acute withdrawal from exposure.

A study by the Navy Environmental Health Center (NEHC) was conducted in 1976 to determine whether personnel exposed to OF II demonstrated any subclinical neurological or cardiovascular effects (18). This study did not find an association between cardiovascular effects and exposure to OF II, although methodologic limitations likely obscured the issue. It did demonstrate neurophysiological effects in personnel exposed to PGDN concentrations as low as 0.1 ppm. The NIOSH criteria document for recommended standards for NG and EGDN likewise indicated that there may be effects on the central nervous system other than headaches, including hallucinations, depression, mania, epilepsy, paresthesias, transient hemiparesias, and aphasia (19).

Other research on NG and EGDN has also shown physiological effects at relatively low concentrations. Steward, et al (20) demonstrated that human exposures to 0.2 ppm or greater produced disruption of the organization of visual evoked response and headaches in a majority of subjects. A tolerance to headaches was noted after repeated 8-hour exposures at 0.2 ppm. Balance impairment was observed after a 6.5 hour exposure to 0.5 ppm. Trainer and Jones (21) found that six of seven workers developed "mild" headaches when exposed to mean concentrations of NG:EGDN vapors of 0.5 mg/m^3 (0.1 ppm) for 25 minutes or less. Blood pressure changes, as well as headaches, were observed in storage magazine workers at inhalation exposures as low as 0.36 mg/m^3 average concentration, with a range from 0.1 to 0.53 mg/m^3 (expressed as NG). Hanlon and Frederick (22) noted headaches and irritation in workers exposed to NG and EGDN at levels of 0.03 - 0.11 ppm and the subsequent disappearance of these symptoms when concentrations were lowered to less than 0.01 ppm. Morikawa, et al (23) reported abnormal pulse waves and headaches in workers exposed at concentra-

tions below 0.1 ppm of NG:EGDN. Horvath, et al (24) clinically evaluated a group of Navy Torpedoman Mates with occupational exposure to OF II. Although there was no evidence of chronic neurotoxicity, transient oculomotor effects were noted after acute exposures below 0.2 ppm.

METHODS

The data used in this investigation were obtained from files provided by the Navy Medical Data Services Center and the Navy Personnel Command. Three study groups were identified: Torpedoman's Mate, potentially exposed to OF II, TM (exposed); Torpedoman's Mates not exposed to OF II, TM (control); and, Fire Control Technicians, FT. The latter two groups were used as internal and external control groups, respectively. Exposure to OF II was determined by PNEC assignment. Torpedoman's Mates were placed in the exposed group when PNEC codes, in the enlisted service history records, indicated that a TM was qualified to work with OF II; these PNEC codes were 0746, 0747, 0748 and 0749. All other TM PNECs comprised the internal control population. All Fire Control Technicians, performing similar technical work as TMs, were selected as an appropriate external control group.

This investigation was divided into two major parts. The time frame for the initial analysis included the years 1966-1979, and encompassed the large group of diagnoses and symptoms that have been shown to be most commonly associated with exposure to nitrated esters.

The second analysis focused the inquiry on conditions such as acute myocardial infarction, angina pectoris and cardiac arrhythmias that historically have been strongly associated with analogous chemical exposures. The study interval covered the 10-year period, 1970-1979, when available occupational identification information (PNEC) best approximated exposure category.

The occurrence of disease in the cardiovascular system was ascertained from inpatient medical files as the first appearance of any of the following selected diagnoses listed on hospitalization, Medical Board, Physical Evaluation Board or death records during the fourteen-year period, 1966-1979. The group of diagnoses and symptoms that have been shown to be most commonly associated with exposure to nitrated esters are listed on the following page.

The distribution of each group was determined by calendar year. TMs not exposed to OF II and FTs were tallied for each year on active duty for the period 1966 through 1979. Active duty starting dates and discharge dates were used for this purpose.

Torpedoman's Mates potentially exposed to OF II however, were tallied for each year on active duty beginning on the date of first assignment of the appropriate PNEC. Otherwise, these TMs were assigned to the TM control group for those years on active duty prior to the first assignment of an OF II PNEC.

Hospitalization (incidence) rates per 100,000 and appropriate confidence limits (25) were then calculated for each study group for each calendar year by dividing the number of events (hospitalizations, Med Boards, PEBs or deaths) by the annual active duty population in each of the occupational groups.

For the initial analysis, survival tables were constructed in order to efficiently summarize the rate of events (probability of survival or its complement, the probability of hospitalization)

ICDA-8 Code	NHRC Code	CVS Diagnosis or Symptom
306.8	286.16	Tension headache
346.0	323.01	Migraine headache
410.0, 410.1, 410.9	390.01 - 390.03	Acute myocardial infarction
411.0, 411.9	391.01 - 391.02	Other acute and subacute forms of ischemic disease
--	394.01	Old myocardial infarction
413.0, 413.9	395.01 - 395.03	Angina pectoris
412.0, 412.9 429.0, 429.9 --	392.01 - 392.02 409.01 - 409.02 410.01 - 410.02	Other forms of chronic ischemic heart disease
427.4 - 427.6	407.05 - 407.09	Cardiac arrhythmias
780.5	729.07	Lightheadedness, vertigo
782.1	731.02	Palpitations
782.5	731.06	Syncope and collapse
783.7	732.08	Chest pain
791.0	739.01	Headache
987.9	932.06	Toxic effects of other gases, vapors, and fumes
989.9	934.07	Toxic effects of other, chiefly nonmedicinal substances
--	935.01	Toxic effects of other substances

over the fourteen-year period (26,27). Survival rate comparisons (based on the cumulative probability of an event occurrence and the standard error of the cumulative probability) were made between the study populations collectively, and by age group.

Also, comparisons of the proportion hospitalized within each of the occupational groups, by age, were made as an estimate of relative risk. Confidence limits were calculated to determine if there were any significant differences between the study groups (28).

In the second analysis, the odds ratio, as an estimate of the relative risk, was used to assess any significant relationships between the exposure groups. Using 2 x 2 tables, the three groups were compared to one another during the two five-year periods (1970-1974 and 1975-1979) and for the entire 10-year span (1970-1979).

The odds ratio was calculated by Woolf's method, which uses the log of the odds ratio, to avoid asymmetry, as a measure of association (29). In this method, 0.5 was added to each cell to correct for bias that can occur with small numbers of observations where the expected value in any cell was less than 5. Ninety-five percent confidence intervals were calculated for the odds ratio (29). When the interval contained the value 1.0, the hypothesis that there was no difference in risk between the two comparison groups was accepted.

RESULTS

First Analysis

Table 1 provides population figures for the three groups upon which the hospitalization (incidence) rates are based. It is noteworthy that the exposed TM population showed steady

increases over the 14-year period while the control TM and FT populations increased through 1969 and then decreased over the next five years followed by a general stabilizing trend for the remainder of the study period. The gradual increases among the exposed TMs may, in part, account for some of the decreases in the TM control population. These subtle shifts may also indicate a more reliable and consistent use of PNECs especially for those TMs working on MK 46 and MK 48 torpedoes.

Other forms of chronic ischemic heart disease accounted for 17% of all CVS related episodes across the study groups as shown in Table 2. Nearly one quarter of all CVS cases were headache related (tension, migraine and generic). Within the exposed TMs, acute myocardial infarcts and other forms of chronic ischemic heart disease each accounted for 29% of the CVS related cases. Other forms of chronic ischemic heart disease was also the most common single diagnosis among TM controls (17.5%) and FTs (15.6%). Episodes of headache (30.6%) and chest pain (15.6%) were also quite common among this group.

Table 3 describes the age distribution across the study groups among those sailors who were hospitalized with at least one of the CVS diagnoses. There is an average four-year age difference between the exposed TMs and FTs, with the TMs being the older group, 28.3 years.

Table 4 and Figure 1 indicate a general increasing trend through 1974 for hospitalization among all TMs and among FTs; long-term trends through 1979 tend to parallel each other. The wide variation between rates for exposed TMs was most likely a result of the small number of hospitalizations that were reported during the study interval. The rates for both exposed and control TMs remained consistently higher than the rates for FTs from 1972 through 1979, however, these differences were not statistically significant.

The most noteworthy characteristic of the hospitalization rates (expressed as rate %) that were based on survival analysis techniques, were the steadily increasing rates as one gets older (Table 5 and Figure 2). Within the individual study groups there were observable differences; unexposed TMs 35 years or older had a significantly higher rate of hospitalization compared to those individuals 29 years or younger; exposed TMs 35 years or older had a significantly higher rate of hospitalization compared to those less than 25 years of age. For the FTs, however, the oldest group had significantly higher rates than for those individuals 29 years or younger, and those 30 to 34 had significantly higher rates than for those less than 25 years of age. There were no significant age-specific differences across the occupational groups.

The proportion of men hospitalized for CVS diagnoses during the seven-year interval 1973-1979 were calculated from the survival data in the life tables. Based on comparisons of these proportions, estimates of relative risk within each age group across the study groups were made and are presented in Table 6 and Figure 3. Although increased risks above 1.0 were apparent when the exposed TM and control TM groups were compared with the FTs, the differences were not significant.

Second Analysis

Table 1 provides population figures (set off by dashed lines) for the three comparison groups for each calendar year (1970-1979), while Table 7 shows the breakdown of specific CVS hospitalizations for the entire 10-year study period.

Table 8 describes the age distribution among TMs and FTs hospitalized with at least one of the three CVS diagnoses. It was apparent that the 35 or greater age group had the largest proportion of cases across all exposure groups. More than 60 percent of the cases in both TM groups and over 52 percent of the FT cases were at least 35 years of age, with the remainder of the cases spread evenly throughout the other age groups.

A summary of the assessment of risk of cardiovascular disease hospitalization among the comparison groups during the 1970-1979 study interval is presented in Table 9. Comparison of 10-year hospitalization rates resulted in odds ratios that were significantly greater than one (1.0) when comparing the exposed TMs to both control groups. These results suggest that over the long-term there was a significant difference in the risk (between comparison groups) of being hospitalized with a CVS diagnosis. Exposed TMs had two and one-half times the risk of a cardiovascular disease outcome compared to the control TM group and four times the risk compared to FTs. When the longer time interval was separated into its two five-year components, there was no difference in risk between the TM groups or between the control TMs and the FTs during both 1970-1974 and 1975-1979. There was, however, a significant difference in risk, during both periods, when the exposed TMs were compared to the FTs. The highest risk (Odds Ratio = 5.25) was noted during the latter period.

DISCUSSION

Theoretically, the best means to investigate the relationships that may exist between chronic exposure to OP II and health effects in TMs would be to conduct a prospective study where one would follow a paradigm that proceeds from cause to effect. A cohort of TMs initially free from disease but who vary in exposure to OP II would be followed over time in a concurrent fashion and observed to determine differences in the rate at which disease develops in relation to exposure. In the present circumstances, the exposed and control groups were traced from some date in the past (1966) up through 1979, and a determination was made of their CVS disease and hospitalization outcome. This type of design is often called nonconcurrent or historical prospective.

After review of the univariate frequency distributions of the 16 cardiovascular, neurologic, and toxic diagnoses within the study groups, they were subsumed into a collective CVS group, which eased data manipulation, reduced potential analytical problems, and promoted more efficient use of computer time. In a like manner, hospitalizations, Medical Boards, Physical Evaluation Boards and Deaths were conveniently grouped together under the term "hospitalization".

The lack of reliable PNEC information prior to 1970, coupled with the small number of CVS hospitalizations within the four OP II PNECs, suggested that TMs should be consolidated into one group for comparative purposes. However, using a combined group of TMs may have diluted the results, therefore, this was not done. The inconsistent use of PNEC information in the late 1960s and early 1970s could have introduced a selection bias by obscuring true exposure experience distinguishing potential OP II workers by PNEC. Coincidentally, at the time these PNECs were coming into common fleetwide use, the temporal trends for CVS hospitalization rates among all TMs and FTs were similar although the rates were higher, in every year, for the TMs.

The sixteen cardiovascular, neurologic, and toxic ICDA-8 Codes are an amalgam of disease conditions and symptoms which might possibly be associated with OF II use. A confounding bias might have been present in that many of these conditions have known non-occupational risk factors and etiologies. The narrowing of the disease conditions and symptoms, in the second analysis, to those most strongly associated with analogous chemical exposures, should have greatly reduced the possibility of this type of bias.

While the initial investigation did not find a statistically significant excess CVS morbidity or mortality in potentially Otto Fuel II exposed TMs, the second analysis indicated that exposed TMs were at a greater risk for CVS disease over the long-term (1970-1979) compared to nonexposed TMs and FTs. This finding is consistent with previous studies which have shown that an increased morbidity is associated with occupational exposure to nitrated ester compounds.

When compared to FTs, both TM groups had an increased risk of cardiovascular disease; the risk being most pronounced for the exposed TMs. This may indicate that all TMs work in an environment which places them at an increased risk of CVS disease; with the exposure to OF II an additional risk factor. Otto Fuel II exposure information would be needed to test this hypothesis and to determine if there is a dose-response effect. Rates and risk assessment based on the few CVS hospitalizations that were observed during these intervals should be interpreted cautiously.

Frequent workplace monitoring and medical surveillance of TMs by Medical Department personnel is recommended so that early symptoms of CVS disease can be detected and treated before disease becomes apparent. Special consideration should be made for individuals who smoke or have close family members with histories of stroke, myocardial infarction, or hypertension.

Currently, attempts are being made to obtain case histories of the afflicted TMs in order to discern any qualitative differences in the type and circumstances of cardiac disease that they experienced.

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TABLE 1

Populations for Otto Fuel II Exposed Torpedoman's Mates and Control Groups for CY 1966-1979

	Occupational Group		
Year	TM (Exposed)*	TM (Control)**	FT
1966	67	4,337	7,943
1967	97	5,272	9,642
1968	161	6,255	11,756
1969	278	7,083	13,659
1970	323	6,933	13,292
1971	366	6,887	12,587
1972	434	6,316	12,087
1973	505	5,549	11,793
1974	572	5,276	11,667
1975	618	5,365	12,065
1976	674	5,195	12,269
1977	769	5,212	12,412
1978	878	5,084	12,412
1979	963	5,072	12,244

*PNEC 0746, 0747, 0748, 0749

**All other TM PNECs

10-year period covered by second analysis

TABLE 2

CVS Hospitalizations Among TMs Exposed and TMs and FTs Not Exposed to Otto Fuel II During CY 1966-1979

CVS Diagnostic Category (ICDA-8)	Occupational Group TM (Exposed)	TM (Control)	FT	Total
Tension Headache	1	6	6	13
Migraine Headache	-	3	17	20
Acute myocardial infarction	4	13	10	27
Other acute and subacute forms of ischemic disease	-	-	1	1
Other forms of chronic ischemic heart disease	4	18	25	47
Old myocardial infarction	-	-	-	-
Angina pectoris	1	6	3	10
Cardiac arrhythmias	1	8	20	29
Lightheadedness, vertigo	1	5	4	10
Palpitation, syncope, collapse	-	12	20	32
Chest pain	-	11	25	36
Headache	1	12	22	35
Toxic effect of other gases, fumes and vapors	1	8	5	14
Toxic effects of other, chiefly non-medicinal substances	-	1	1	2
Other substances	-	-	1	1
Total	14	103	160	277

TABLE 3

Age Distribution Among TMs Exposed to Otto Fuel II, TMs and FTs Not Exposed for Hospitalizations* in Selected (CVS) Diagnoses for CY 1966-1979

Age Group	Occupational Group TM (Exposed)	TM (Control)	FT
≤19	2	33	52
20 - 24	4	21	49
25 - 29	3	19	25
30 - 34	2	13	17
≥35	3	17	17
Total	14	103	160
Mean Age	28.3	26.0	24.3
(S.D.)	(8.4)	(8.2)	(6.8)

*The generic term hospitalizations includes hospitalizations, Medical Boards, Physical Evaluation Boards and Deaths within the Cardiovascular System (CVS) sphere of diagnoses.

TABLE 4

Hospitalization Rates for Selected CVS Diagnoses Among TMs Exposed to Otto Fuel II and TMs and FTs Not Exposed During CY 1966-1979

	Occupational Group								
	TM (Exposed)			TM (Control)			FT		
Year	No. Hosp.	Rate*	C.I.**	No. Hosp.	Rate	C.I.	No. Hosp.	Rate	C.I.
1966	-	-	-	2	46	6,166	3	38	8,111
1967	-	-	-	5	95	31,221	6	62	23,135
1968	-	-	-	2	32	27,116	7	60	25,124
1969	-	-	-	5	71	23,166	10	73	35,134
1970	1	310	8,1727	10	144	69,265	16	129	69,194
1971	1	273	7,1521	7	102	41,210	17	135	79,216
1972	1	230	6,1281	14	222	121,373	14	116	63,195
1973	2	396	48,1430	7	126	51,260	8	68	29,134
1974	1	175	4, 975	12	227	117,397	19	163	98,254
1975	1	162	4, 902	11	205	103,367	13	108	58,185
1976	2	297	36,1072	6	116	43,253	12	98	51,172
1977	1	130	3, 724	9	173	79,329	14	113	62,190
1978	3	342	70, 998	6	118	43,257	9	73	33,139
1979	1	104	3, 579	7	138	55,284	12	98	51,172
Totals	14	209	114, 351	103	129	106,157	160	96	82,113

*Number of hospitalizations in CVS diagnostic groups / Annual population in occupational group

**95% Confidence interval based on Lilienteld (1980)[25]

TABLE 5

Number of Hospitalizations, Rate of Hospitalization for Selected CVS Diagnoses, with 95% Confidence Intervals, by Occupational Group and Age During CY 1966-1979

	Occupational Group											
Age	TM (Exposed)				TM (Control)				FT			
Group	No.	Rate(%)*	S.E.	C.I.**	No.	Rate(%)	S.E.	C.I.	No.	Rate (%)	S.E.	C.I.
≤19	2	0.8	.006	.1,2.9	33	2.5	.009	1.7,3.5	52	0.9	.002	.7,1.1
20-24	4	2.2	.011	.6,5.7	21	2.3	.006	1.4,3.5	49	2.1	.004	1.6,2.5
25-29	3	2.6	.016	.5,7.6	19	3.4	.008	2.0,5.2	25	3.2	.007	2.0,4.7
30-34	2	3.1	.021	.4,11.1	13	5.9	.021	3.1,10.0	17	5.8	.016	3.4,9.1
≥35	3	33.3	.157	6.9,47.3	17	12.5	.037	7.3,20.0	17	11.2	.033	6.6,11.4
Totals	14	2.7	.008	1.5,4.5	103	3.4	.004	2.8,4.1	160	2.3	.003	2.0,2.7

*Derived from life table analysis techniques described by Berkson and Gage (26) and presented in SPSS-X (27) where

Rate (%) = (1 - Cumulative proportion surviving in specific group at end of interval) X 100

**95% Confidence Interval Based on Lilienfeld (25)

TABLE 6

Estimation of Relative Risk, by Age Based on Comparison of Proportion Hospitalized Among TMs Exposed to Otto Fuel II and TMs and FTs Not Exposed; 1973-1979

Age Group	Cumulative Proportion Hospitalized TM (Exp)	TM (Cont)	FT	Relative Risk (95% Confidence Interval)* RR^a	RR^b
≤ 19	.0046	.0052	.0054	.88	.85
20-24	.0054	.0090	.0049	.60	1.10
25-29	.0049	.0120	.0091	.41	.54
30-34	.0296	.0296	.0209	1.00	1.42 (.49,4.13)
≥ 35	.0651	.0353	.0254	1.84 (.61,5.52)	2.56 (.85,7.69)

a $\frac{\text{Proportion Hospitalized - TM (Exp)}}{\text{Proportion Hospitalized - TM (Cont)}}$

b $\frac{\text{Proportion Hospitalized - TM (Exp)}}{\text{Proportion Hospitalized - FT}}$

* $C.I. = \ln(RR) \pm 1.96\sqrt{\frac{1-P_1}{n_1} + \frac{1-P_2}{n_2}}$ Katz, et al(28)

TABLE 7

Hospitalization Among TMs Exposed and TMs and FTs Not Exposed to Otto Fuel II for Selected CVS Diagnoses During CY 1970-1979

CVS Diagnostic Category (ICDA-8)	TM (Exposed)	TM (Control)	FT
Acute Myocardial Infarction	5	17	15
Angina pectoris	1	5	8
Cardiac arrhythmias	2	9	19
Total	8	31	42

TABLE 8

Age Distribution Among CVS Hospitalized TMs Exposed to Otto Fuel II and TMs and FTs Not Exposed During CY 1970-1979

Age Group	TM (Exposed)	TM (Control)	FT
≤ 19	-	2	-
20 - 24	1	2	6
25 - 29	1	3	4
30 - 34	1	5	10
≥ 35	5	19	22
Total	8	31	42
Mean Age (S.D.)	32.9 (6.5)	35.8 (8.9)	34.7 (10.9)

TABLE 9

Calculation of Odds Ratios and Confidence Intervals for TMs Exposed and TMs and FTs Not Exposed to Otto Fuel II During CY 1970-1979

Comparison Group	Observation Period	Odds Ratio*	Confidence Interval**
TM (Exposed) vs TM (Control)			
	1970-1974	2.66	0.78, 9.04
	1975-1979	2.71	0.97, 7.60
	1970-1979	2.52	1.16, 5.48
TM (Exposed) vs FT			
	1970-1974	3.69	1.12,12.20
	1975-1979	5.25	1.92,14.34
	1970-1979	4.03	1.89, 8.59
TM (Control) vs FT			
	1970-1974	1.37	0.75, 2.50
	1975-1979	1.92	0.93, 3.94
	1970-1979	1.59	1.00, 2.53

*Woolf's method: $\ln[(a + 0.5)(d + 0.5)/(b + 0.5)(c + 0.5)] = \hat{\omega}_h$

(29) $\hat{\psi}_h = \exp(\hat{\omega}_h) = (a + 0.5)(d + 0.5)/(b + 0.5)(c + 0.5)$

**95% Confidence intervals (29):

$$\ln \hat{\psi} \pm 1.96 \sqrt{(1/a + 1/b + 1/c + 1/d)}$$

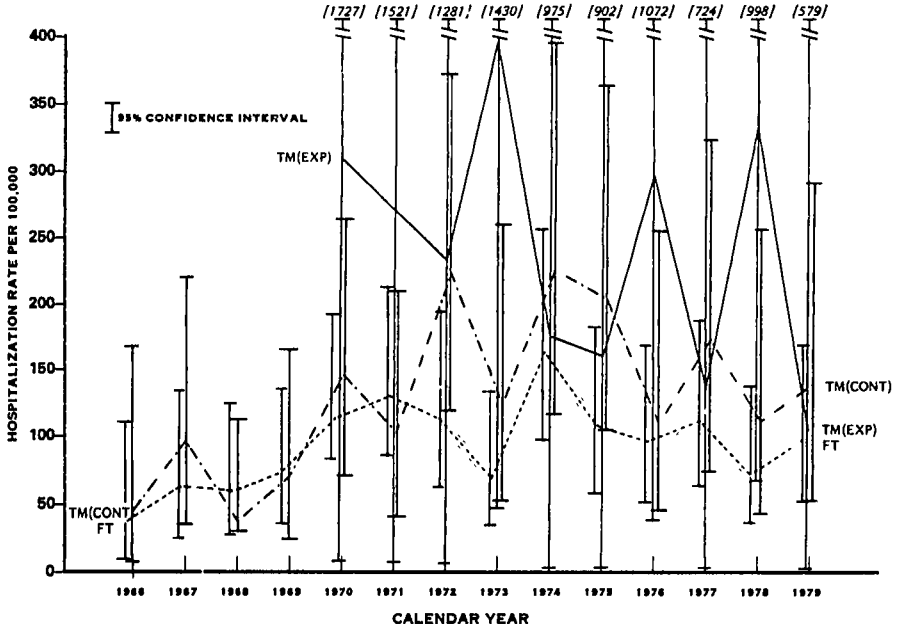

Figure 1. Hospitalization rates for selected CVS diagnoses among Torpedoman's Mates and Fire Control Technicians during CY 1966-79

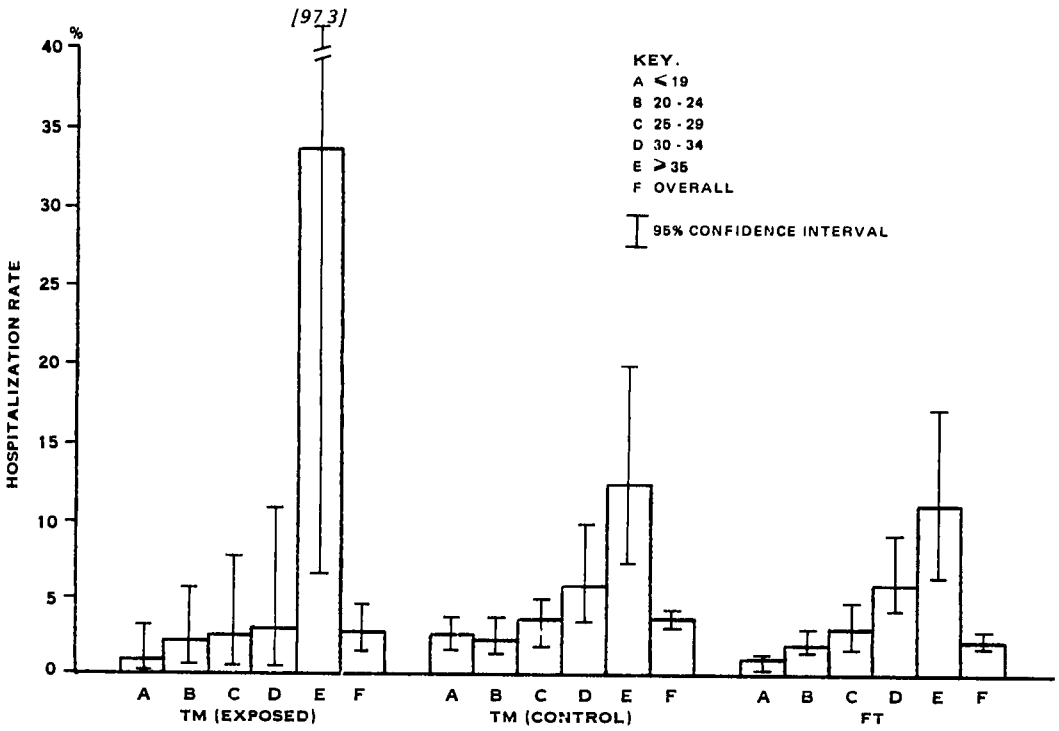

Figure 2. Rate of hospitalization for selected CVS diagnoses by age and occupational group during CY 1966-79.

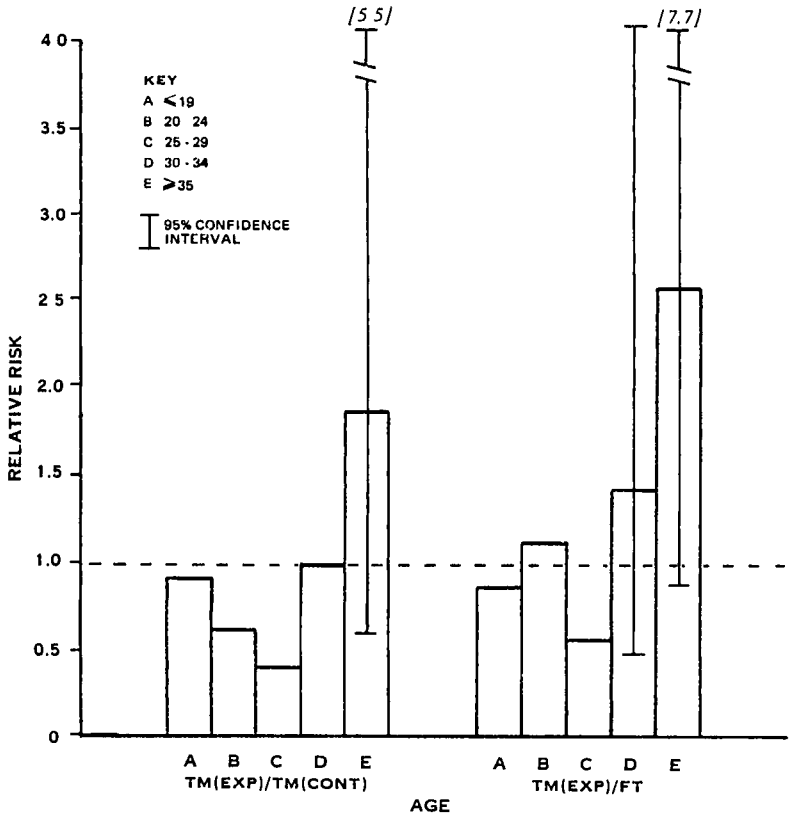

Figure 3. Relative risk, by age, among Torpedoman's Mates exposed to Otto Fuel II and Fire Control Technicians not exposed during CY 1973-79.

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20 ABSTRACT (Continue on reverse side if necessary and identify by block number)

This investigation assessed whether the morbidity and mortality previously associated with nitrated esters would be found in Torpedoman's Mates (TM) potentially exposed to Otto Fuel II. In the initial analysis, illness and/or death in 16 selected cardiovascular, neurologic, and toxic diagnoses were compared among potentially exposed TMs (and appropriate control groups) during the period 1966-1979. Hospitalization rates and confidence intervals were calculated and survival tables were used to calculate the probability of hospitalization. Estimates of age and occupational group-specific relative

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risks were then made to determine if there were any significant risk differences between the study groups. There was no statistically significant excess of CVS morbidity or mortality in TMs. Lack of reliable PNEC information prior to 1970 may have introduced a selection bias that obscured the true Otto Fuel exposure experience of TMs. Additionally, the wide spectrum of disease conditions that may be associated with the use of Otto Fuel have known non-occupational risk factors and etiologies that could be confounding factors.

To overcome these biases, a second analysis focused on three CVS conditions (acute myocardial infarction, angina pectoris and cardiac arryhthmias), known to be associated with analogous nitrated esters. Risk assessment analysis for the ten-year period (1970-1979) suggests that exposed TMs have a significantly greater risk of a CVS related hospitalization compared to other TMs and FTs.