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**Aviation Epidemiology Data Register:
Cardiovascular Disease Screening Outcomes
in the North Dakota
Army National Guard Aviator Cohort**

By

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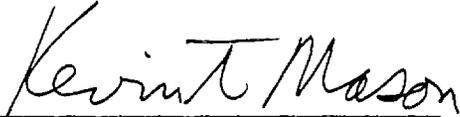
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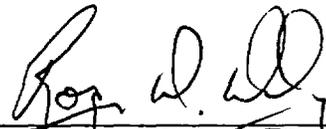
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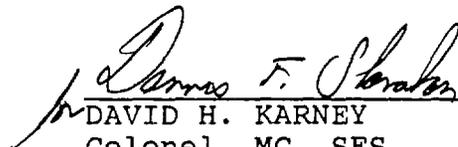


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were significantly older and had been exposed to more years in level 1 screening at age 40 and older than other ARNG aviators. The NDARNG aviators had higher total cholesterols, significantly lower high density lipoprotein (HDL) cholesterols, and significantly higher total cholesterol and HDL cholesterol ratios, all of which contributed to an increased risk for level 1 failure.

Since NDARNG aviators were more likely to fail level 1 screening, they were more likely to enter level 2 cardiovascular disease detection screening. NDARNG aviators who entered level 2 screening were at increased risk for failing level 2 screening compared to other ARNG aviators, although the degree of increased risk was not statistically significant. Therefore, NDARNG aviators were not significantly at risk for referral for diagnostic aeromedical cardiac catheterization in the screening program.

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Introduction

Responding to a Congressional inquiry, the U.S. Army Surgeon General's office directed, "A study to determine whether or not North Dakota Army National Guard aviators undergo cardiac catheterization in disproportionate numbers compared to what would be expected in a similar population." The Aviation Epidemiology Data Register was queried to answer the request.

Aeromedical cardiovascular disease screening program

U.S. Army aircrew members participate in the aeromedical cardiovascular disease screening program (ACVDSP) during their annual flying duty medical examination (FDME) for the prevention and detection of cardiovascular diseases. Prevention is the cornerstone of the program, but in aircrew members, it is desirable to detect significant disease before symptoms occur. Multiple factors shown in Table 1 form the basis of decision for the detection aspect of the ACVDSP (Gordon, Sorlie, and Kannel, 1971; Kannel et al., 1975; Dark, 1983; Hickman, 1987; Kannel and McGee, 1985; Copeland, 1987; Booze, 1989).

Table 1.
Factors associated with cardiovascular disease in Army aircrew members.

Factor	Implication
Cardiovascular disease is the leading cause of sudden, premature death in the U.S.	Major public health problem
Cardiovascular disease is the leading cause of premature medical suspension from flying duty careers worldwide	Major aviation medicine problem
Cardiovascular disease causes acute incapacitation (sudden death, chest pain, etc.) usually without warning	Personal safety and health hazard
Acute onset of cardiovascular disease symptoms is associated with aircraft mishaps in a majority of events	Potential aviation and public safety hazard
Poor cardiovascular health degrades a soldier's ability to complete military missions	Preventive medicine efforts can help maintain the air warrior's health and readiness

The main focus of the ACVDSP is reduction of cardiovascular disease risk factors. All aircrew members, regardless of age, are screened for cardiovascular disease risk factors. Army flight surgeons reduce elevated risk factors that are amenable to modification such as smoking habit, hypertension, or elevated serum cholesterol. The long-term goal is to decrease the incidence of cardiovascular disease complications in aircrew members.

Aircrew members who are 40 years or older participate in a cardiovascular disease detection program (Appendix A; Department of the Army, 1991a). The ACVDSP uses a stratified approach with two levels of screening (levels 1 and 2) and, if required, two levels of diagnostic testing (levels 3 and 4). In the primary level of screening (level 1), cardiovascular disease risk factors are evaluated. Factors evaluated include age, smoking and cardiac history, blood pressure, blood sugar, lipid profile, and resting electrocardiogram. In level 1 screening, aircrew members are divided into low and high risk groups for the risk of developing cardiovascular disease. High risk personnel are referred for management of elevated risk factors. Those at high risk are referred for secondary screening tests (level 2). Those at highest risk for having cardiovascular disease in level 2 are referred to aeromedical cardiologists for diagnostic testing (levels 3 and 4). Table 2 shows the factors assessed in ACVDSP level 1 and level 2. Level 4 diagnostic evaluation usually includes coronary angiography. Test results are reviewed to measure the degree of cardiovascular disease and make flying duty recommendations to the Commander, U.S. Army Aeromedical Center.

Based on advancing age alone, all aviators eventually will either leave the cohort (retirement, disease, death, etc.) or fail level 1 screening. Advancing age is an independent, significant risk factor for the presence of asymptomatic or symptomatic cardiovascular disease. Only those 40 years and older are subject to level 2 screening, which places them at risk for level 2 screening failure and referral to aeromedical cardiology consultation for possible coronary angiography.

Aviation Epidemiology Data Register

The Aviation Epidemiology Data Register (AEDR) is a family of databases that stores the health history and physical parameters of Army aircrew members. One component stores FDMEs from 1985 to the present. This database is linked by Social Security number to the waiver and suspense file (WSF), which is an index of major diseases and injuries found in Army aircrew members. The WSF is referenced to a medical document image archive that stores the medical records related to each diagnosis or injury.

Table 2.
Factors assessed in level 1 and level 2 screening*

Level	Factor	Pass	Fail
1	History	No symptoms	Symptoms, referred for clinical evaluation and care
	Resting ECG	No serial changes	Serial changes, workup as per APL 2**, ECG findings, some cases referred to level 2 screening as required
	Framingham risk index (See Appendix B)	<5.0%	>=5.0%, referred to level 2 screening
	Total cholesterol	<270 mg/dl	>=270 mg/dl, referred to level 2 screening
	Cholesterol/HDL ratio	<6.0	>=6.0, referred to level 2 screening
2	Graded exercise treadmill test	Normal, modify risk factors	Abnormal, >=1.0 mm ST depression any lead or stress arrhythmias, referred for diagnostic testing
	Cardiac fluoroscopy	Normal, modify risk factors	Cardiac calcifications present, referred for diagnostic testing

* See Aeromedical Policy Letter 28-91 (Department of the Army, 1991a).

** See Aeromedical Policy Letter 2-89 (Department of the Army, 1989).

Method

There are significant age differences between active duty, Army Reserve, and Army National Guard (ARNG) aviators (Mason and Shannon, 1994), confounding the use of all Army aviators as a comparison group. Therefore, all other ARNG aviators were selected for members of the comparison population.

The AEDR retrospectively was queried to extract all data on individuals who had at least one FDME as an ARNG aviator between 1988 and 1993. This group further was divided into those assigned to current and historical aviation units of the North Dakota Army National Guard (NDARNG) and those in ARNG units other than NDARNG during the study period.

Parameters from their FDMEs were tabulated and compared by univariate analysis using SAS® PROC FREQ and SAS® PROC NPARIWAY (SAS Institute, 1990; SAS Institute, 1994; Daniel, 1983). Parameters reviewed included age, total serum cholesterol, HDL cholesterol, cholesterol/HDL ratio, fasting blood sugar, height, weight, body mass index, systolic and diastolic blood pressure, pulse, visual acuity, and hearing acuity in multiple frequencies. Smoking history significantly and adversely affects the Framingham Risk Index value. Since smoking histories could not be extracted reliably from FDME histories, a comparison of smoking histories was not done.

The AEDR waiver and suspense file was queried to find the ACVDSP outcomes of all ARNG aviators in this study. Questionable or incomplete waiver and suspense file entries were resolved by reviewing the medical document archive file for each case. Cardiovascular disease outcomes for those aviators who were 40 years or older during the study period were stratified into groups based on pass/fail for each level of the ACVDSP. The strength of association between membership in the NDARNG and ACVDSP outcomes was assessed using a relative risk estimate. Variances and 95 percent confidence intervals of the estimated relative risk were calculated by the method of Katz (Kahn and Sempos, 1989; Kelsey, Thompson, and Evans, 1986).

Due to the small sample size of the NDARNG, a matched pair, case-control method was used to adjust for the effect of some possible confounding variables. For each member of the NDARNG cohort who had at least one FDME at 40 years old or older during the study period, a control from the non-NDARNG cohort was selected who had the same age, years of exposure to level 1 screening at 40 years old or older, total cholesterol to HDL-cholesterol ratio, and total cholesterol. Odds ratio and 95 percent confidence intervals for the matched pair, case-control study were calculated by the method of Miettinen (Kahn and Sempos, 1989).

Results

During the period for 1 January 1988 through 31 December 1993, there were 48 aviators in the NDARNG and 9699 aviators in all other ARNG units who completed at least one ARNG FDME. Only those 40 years old or older were at risk for entering the ACVDSP disease detection screening, so the two groups were stratified by age beginning at 40 years old. The younger aviators who were less than 40 were dropped from the cohort, leaving 28 NDARNG aviators and 4699 aviators in other ARNG units who became 40 or older during the study period. Table 3 shows the number of aviators who were 40 or older during at least 1 year in the study period, the number of aviator-years of exposure to level 1 of the screening program, mean years of exposure, and rate of level 1 failure per 1,000 aviator-years of exposure to screening.

ARNG aviators failed level 1 at a rate of 108.7 NDARNG aviators per 1,000 aviator-years of exposure to screening as compared to 53.9 non-NDARNG aviators per 1,000 aviator-years of exposure. The average NDARNG aviator was exposed to 4.9 years of level 1 screening compared to 3.6 years of screening for other ARNG aviators. Table 4 shows the relative risk of ARNG aviators failing level 1 of the cardiovascular disease screening. NDARNG aviators were significantly more likely to fail level 1 ACVDSP screening. The relative risk was 2.74 (95 percent CI of 1.93, 3.88).

Of the 15 NDARNG aviators who failed level 1 screening, all completed level 2 screening at the time of this study. Of the 920 other ARNG aviators who failed level 1 screening, only 659 had completed level 2 screening. Of those not completing level 2 screening (261), 106 retired from aviation service before completing level 2 screening and 155 had level 2 screening evaluations pending at the time of this study. Table 5 shows the relative risk of level 2 screening failure for those completing level 2 screening. NDARNG aviators were more likely to fail level 2 screening with a relative risk was 2.22 (95 percent CI of 1.06, 4.64). This increase risk was not statistically significant.

Table 6 shows an analysis of factors associated with passing or failing level 1 in 1992. Factors analyzed included age, total cholesterol, HDL-cholesterol, and total cholesterol to HDL-cholesterol ratio. These factors contributed to NDARNG aviators higher risk for failing level 1 cardiovascular disease screening. Other factors not in Table 6, including fasting blood sugar, height, weight, body mass index, systolic and diastolic blood pressure, pulse, visual acuity in both eyes, and hearing acuity in both ears and in multiple frequencies, were not significantly different between the two populations, nor did they contribute to failure of level 1.

Table 3.
Rate of level 1 failure among ARNG aviators for calendar years 1988 to 1993.

Factor	Cohort	
	NDARNG aviators	Other ARNG aviators
Age \geq 40 (N)	28.0	4699.0
Aviator-years of exposure to level 1 screening	138.0	17074.0
Mean years of exposure per aviator	4.9	3.6
Failed level 1 (N)	15.0	920.0
Level 1 failure rate per 1,000 aviators	108.7	53.9

Table 4.
Relative risk of level 1 screening failure among ARNG aviators.*

Cohort	Fail level 1 screening	Pass level 1 screening	N
NDARNG aviators	15	13	28
Other ARNG aviators	920	3799	4699

* Relative risk of 2.74 (CI_{95%} of 1.93, 3.88).

Table 5.
Relative risk of level 2 screening failure among ARNG aviators.*

	Fail level 2 screening	Pass level 2 screening	N
NDARNG aviators	5	10	15
Other ARNG aviators	99	560	659

* Relative risk of 2.22 (CI_{95%} of 1.06, 4.64).

Table 6.
Comparison of selected cardiovascular disease screening risk factors in 1992.

Factor	Age \geq 40 years old	
	NDARNG aviators	Other ARNG aviators
Age		
Mean	47.22	45.77
t-test	p=0.044*	
Cholesterol		
Mean	206.36	203.90
t-test	p=0.729	
HDL cholesterol		
Mean	39.05	44.85
t-test	p=0.019*	
Cholesterol/HDL ratio		
Mean		
t-test	5.95 p<0.001*	4.79

* The difference between NDARNG and other ARNG aviators is significant ($p < 0.05$).

NDARNG aviators were significantly older than other ARNG aviators. NDARNG aviators had higher total serum cholesterols. Although this difference did not reach statistical significance, a higher cholesterol increases the screening Framingham Risk Index value and contributes to an increased risk for failing level 1 screening (Table 2 and Appendix B). NDARNG aviators also had significantly lower HDL-cholesterols and significantly higher total cholesterol to HDL-cholesterol ratios. Figures 1 through 4 show the cumulative frequency distribution of these factors.

Controlling for the increased risk factors and increased risk for failing level 1, 13 matched pair case-controls were found to have entered level 2 screening. Despite controlling for age, years of exposure to level 1 screening, and cholesterol profiles, NDARNG aviators were at increased risk for failing level 2 (abnormal graded exercise treadmill test and/or abnormal cardiac fluoroscopy) with an odds ratio of 4.0 (95 percent CI of 0.192, 83.4). This increased risk was not statistically significant (Table 7).

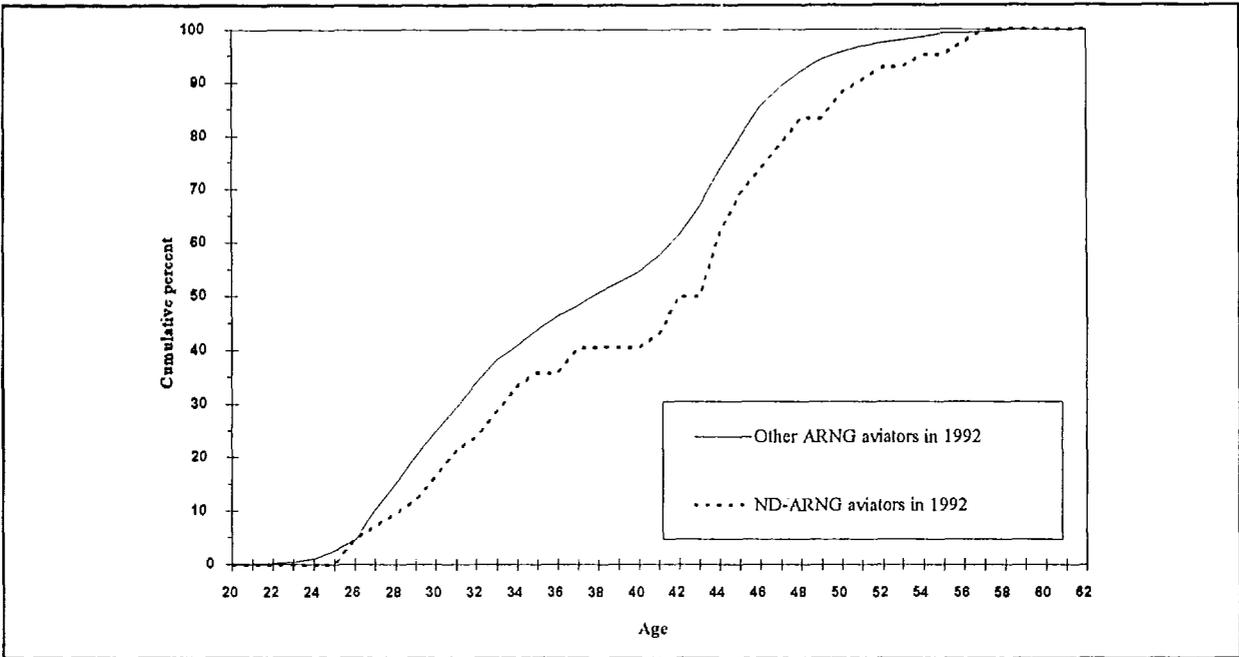


Figure 1. Cumulative frequency distributions of ages for NDARNG aviators compared to other ARNG aviators.

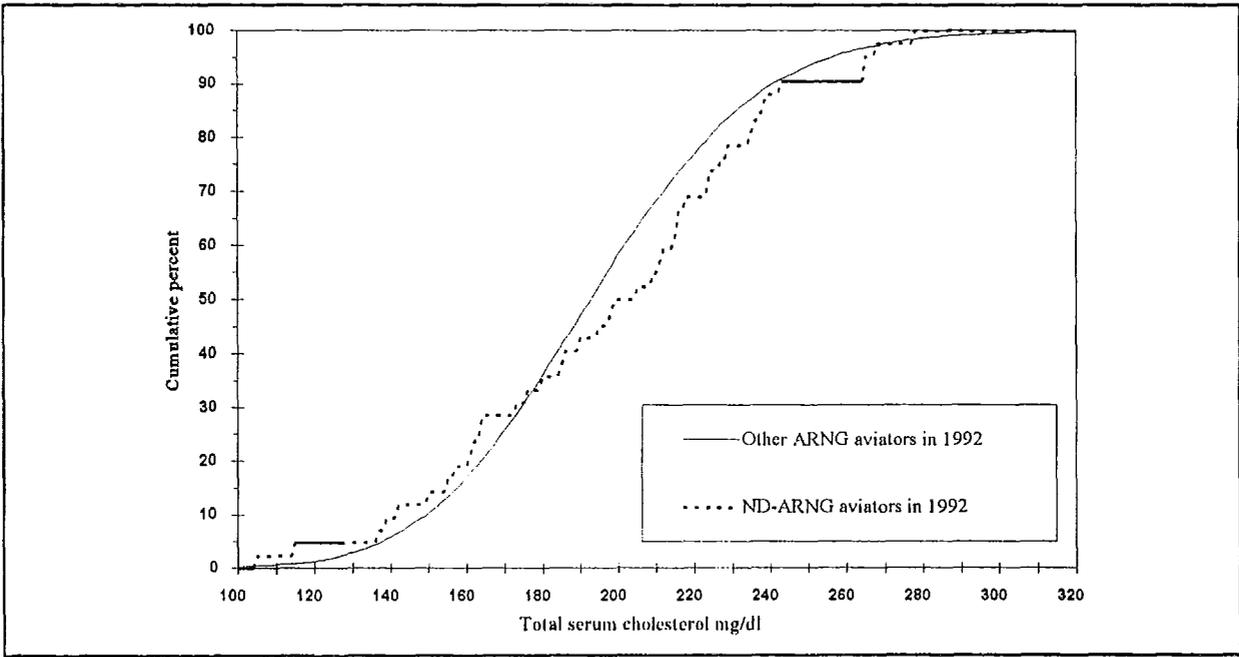


Figure 2. Cumulative frequency distributions of total serum cholesterols for NDARNG aviators compared to other ARNG aviators.

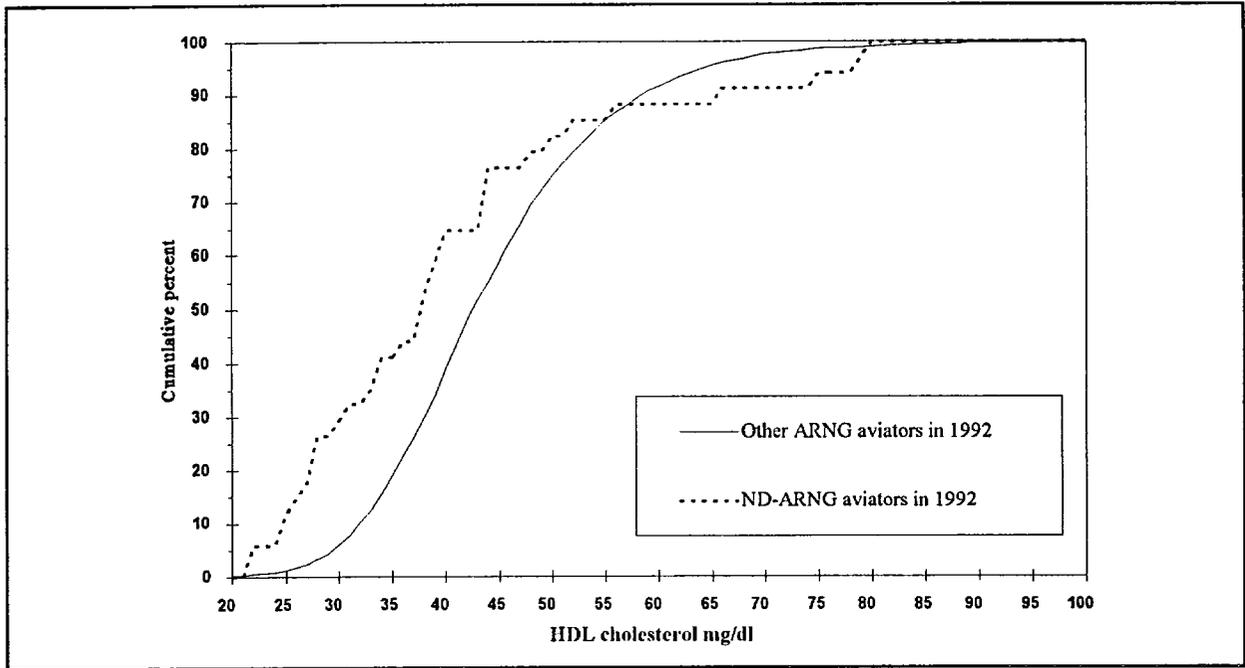


Figure 3. Cumulative frequency distributions of HDL-cholesterols for NDARNG aviators compared to other ARNG aviators.

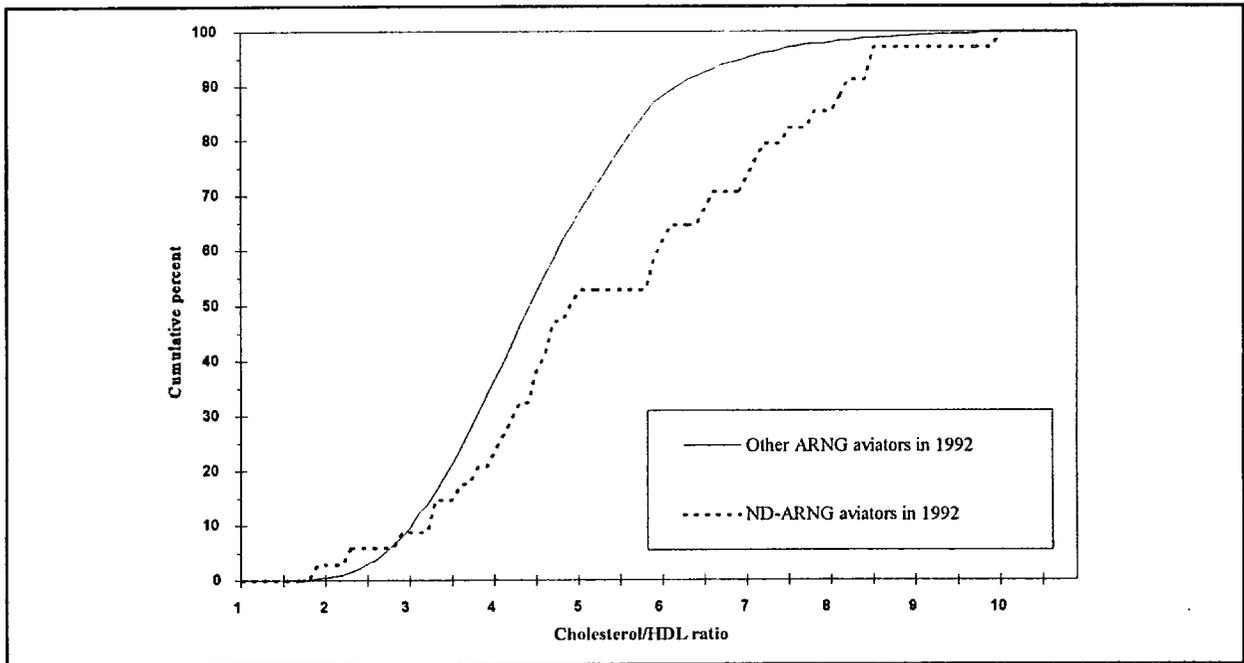


Figure 4. Cumulative frequency distributions of total cholesterol to HDL-cholesterol ratios for NDARNG aviators compared to other ARNG aviators.

Table 7.
Matched pair case-control study of level 2 failures*.

Case (NDARNG)	Control (Other ARNG)		N
	Fail level 2	Pass level 2	
Fail level 2	1	4	5
Pass level 2	1	10	11
N	2	14	16

* Odds ratio_(matched pair) of 4.0 (CI_{95%} of 0.192, 83.4).

Discussion

A review of the NDARNG aviator cohort showed they were a stable population. A majority (42 of 48) remained in NDARNG aviation service for all 7 years of this study. NDARNG aviators are significantly older than other ARNG aviators. Since entering level 1 screening is dependent on an aviator being 40 years old or older, the older age and population stability both resulted in the average NDARNG aviator being exposed to more aviator-years of level 1 screening than other ARNG aviators (4.93 mean years versus 3.63 mean years).

Failure of level 1 is dependent on factors listed in Table 2. Appendix B shows the Framingham Risk Index is greatly influenced by age and total cholesterol values. Based on the differences in the mean age and total cholesterol observed in this study, the Framingham Risk Index would increase by 33 percent in the NDARNG cohort compared to other ARNG aviators.

Failure of level 1 screening also is dependent on the total cholesterol to HDL-cholesterol ratio. NDARNG aviators had a significantly higher total cholesterol to HDL-cholesterol ratios than other ARNG aviators. Based on the mean total cholesterol to HDL-cholesterol ratio of 5.95 for the NDARNG aviators who were 40 or older in 1992, nearly half would fail level 1 using the criteria in Table 2.

Among those ARNG aviators failing level 1 screening, NDARNG aviators are at increased risk for failing level 2 screening, even when controlling for population differences. This increase in risk was not statistically significant. However, the failure to achieve statistical significance likely was due to the small sample size of the NDARNG (only 15 NDARNG aviators failed level 1 and five failed level 2), which greatly increased the variance of findings. It is failure of level 2 screening that results in referral to aeromedical cardiologists who might recommend diagnostic aeromedical cardiac catheterization based on the finding of additional noninvasive diagnostic tests.

During the study period, five NDARNG aviators failed level 2 screening. Four underwent cardiac catheterization, and one was referred recently for possible cardiac catheterization. Based on ARNG-wide experience tabulated in this study, half of the NDARNG aviators undergoing catheterization should have coronary artery disease of a degree to end their flying careers. Fortunately to date, the NDARNG experience is better than other ARNG units. All four NDARNG aviators undergoing catheterization were returned to flying duties, two with normal findings, and two with minimal degrees of coronary artery occlusions.

Two possible confounding variables were not assessed. The first variable is smoking history. A history of smoking increases the risk for failing level 1 by elevating the Framingham Risk Index (Appendix B). A history of smoking increases the risk for cardiovascular disease complications. Unfortunately, the smoking history is not reported reliably on the FDME. We know from practical experience, some aviators conceal their smoking history to make a more favorable impression of good health practices during a FDME, avoiding the smoking cessation lecture by the flight surgeon.

The second possible confounding variable is unknown cardiovascular disease screening outcomes. All NDARNG aviators completed level 2 screening if they failed level 1. However among other ARNG units, the results of level 2 screening are unknown among 261 of 920 (28.4 percent) aviators who failed level 1. Of these 261, 155 have level 2 evaluations pending while in aviation service, and the other 106 retired before completing level 2. Among these 261 unknown cases, it is uncertain how many would have failed level 2, resulting in referral for cardiac catheterization. The potential bias is that some of these aviators may chose to avoid further evaluation because of factors such as a strong family history of cardiac disease or based on the results of private cardiology consultation. We are aware that at least one ARNG retiree had a myocardial infarction shortly after declining level 2 evaluation and retiring. Even a few catheterizations in this unknown group could significantly tip the balance of this study and strengthen the notion that the NDARNG experience is likely the same as other ARNG peers.

Conclusions

This study compared the aeromedical cardiovascular disease screening outcomes between the North Dakota Army National Guard aviator cohort and a peer cohort of all other ARNG aviators. The comparison was conducted on aviators who were age 40 and older, which is the age aviators enter a cardiovascular disease screening program for cardiovascular disease detection.

NDARNG aviators were significantly more likely to fail level 1 cardiovascular disease screening due to multiple, related factors. NDARNG aviators were significantly older and had more screening exposure-years at 40 years and older in level 1 screening than other ARNG aviators. NDARNG aviators had higher total serum cholesterols increasing the risk for level 1 failure. NDARNG aviators also had significantly lower HDL-cholesterols and significantly higher total cholesterol to HDL-cholesterol ratios. If the NDARNG did not have significant increases in key level 1 risk factors, we would anticipate their risk of failing level 1 would be the same as the rest of the ARNG aviator work force based on the findings of a matched pair, case-control study.

Since NDARNG aviators were more likely to fail level 1 screening, they were more likely to enter level 2 cardiovascular disease detection screening. NDARNG aviators who entered level 2 screening were at increased risk for failing level 2 screening, but this increase risk was not statistically significant. Therefore, NDARNG aviators were not significantly at increased risk for referral for diagnostic aeromedical cardiac catheterization in the ACVDSP. However, failure to attain statistical significance may be due to the very small size of the NDARNG unit.

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Appendix A.

U.S. Army Aeromedical Cardiovascular Disease Screening Program: principles and guidelines

General principle

The principle of the U.S. Army aeromedical cardiovascular disease screening program (ACVDSP) is multiple level stratification of aircrew members based on risk assessment and test findings. First, Army aircrew members are stratified into low and high risk groups for the likelihood of developing cardiovascular disease by assessment of risk factors using history and physical findings. Only aircrew members found to be at high risk in the primary screening are referred for the second level of noninvasive screening tests (Department of the Army, 1991a). The intent is to use Bayesian theory and enhance the predictive value of the second level screening tests by applying the tests only to a population with a theoretical higher prevalence of underlying disease (Hickman, 1987).

Level 1

Level 1 is the primary level of stratification for screening. Aircrew members are asked questions relating to their cardiovascular system history, to include smoking history. They undergo a resting electrocardiogram (EKG), which is compared to previous tracings. Serum lipids are evaluated, with total cholesterol (T-CHOL) and high density lipoprotein cholesterol (HDL-CHOL) required as a minimum. Their Framingham Risk Index is calculated by the method in Appendix B.

Aircrew members with signs and symptoms of cardiovascular disease, such as exertional chest pressure or serial EKG changes, are considered as screening program failures. They are referred for clinical care and evaluation as symptomatic patients.

Asymptomatic aircrew members are divided into low and high risk groups for the likelihood of developing cardiovascular disease by assessment of risk factors. High risk aircrew members are those who are 40 years old and older; and who have a Framingham Risk Index of 5.0 percent or greater, or a serum T-CHOL 270 mg/dl or greater, or a ratio of the serum T-CHOL over the serum HDL-CHOL of 6.0 or greater. High risk aircrew members are referred for secondary level of screening in level 2.

Level 2

Asymptomatic aircrew members at high risk by level 1 screening are referred for secondary screening. Secondary screening tests are graded exercise treadmill test and cardiac fluoroscopy. The graded exercise treadmill test is abnormal if there is greater than or equal to 1.0 mm ST segment depression in any of 12 leads in any 3 consecutive heart beats at any time during the test. Certain exercise induced electrocardiographic arrhythmias, such as ventricular or supraventricular tachycardia, or left bundle branch block, also are abnormal findings (Department of the Army, 1989). The cardiac fluoroscopy is abnormal if any degree of calcification is seen moving synchronously with the heart shadow in a location consistent with coronary artery anatomy by multiple views (Department of the Army, 1991b; Mason and Shannon, 1993; Mason, 1993). Aircrew members with one or more level 2 screening abnormalities are referred for occupational, diagnostic evaluation in level 3 and 4.

Level 3

Aircrew members entering level 3 are referred for noninvasive testing. The tests include 24 hour Holter monitor testing, echocardiogram, and thallium scan. Abnormalities found by these tests may result in medical termination of aviation service, and thus, may be a contraindication for referring the aircrew member to level 4, invasive diagnostic testing. The most common contraindications found by level 3 testing are recurrent, aeromedically significant electrocardiographic arrhythmias and left ventricular hypertrophy (Mason, 1992).

Level 4

Aircrew members entering level 4 are referred for occupational, invasive diagnostic testing. The tests include left heart catheterization with coronary angiography and left ventriculography (Mason, 1992). Electrophysiologic studies are performed as indicated.

Appendix B.
Framingham Risk Index calculation method.

$$\text{Framingham Risk Index} = \frac{1}{1 + e^{-\text{coeff}}}$$

The variable "coeff" is the total beta coefficient and is derived from the multiple logistic regression analysis formula (Gordon, Sorlie, and Kannel, 1971):

$$\begin{aligned} \text{total beta coeff} = & \beta_0^* + (\beta_1 \times \text{age}) + (\beta_2 \times \text{age}^2) + \\ & (\beta_3 \times \text{age} \times \text{total cholesterol in mg/dl}) + (\beta_4 \times \text{total cholesterol in mg/dl}) + \\ & (\beta_5 \times \text{systolic blood pressure in mmHg}) + \\ & (\beta_6 \times \text{smoking history}^{**}) + \\ & (\beta_7 \times \text{LVH on electrocardiogram}^{***}) + \\ & (\beta_8 \times \text{diabetes}^{****}) \end{aligned}$$

Table B-1.
Framingham Risk Index beta coefficients by gender.

Factor	Gender is male	Gender is female
β0	-22.227532	-19.066572
β1	0.460575	0.311558
β2	-0.002882	-0.001724
β3	-0.002882	-0.001724
β4	0.028590	0.016802
β5	0.012444	0.015278
β6	0.447815	0.049966
β7	0.743158	0.441707
β8	0.265016	0.416906

Notes:

* Factors "β0" through "β8" are gender adjusted and are listed in Table C-1.

** For the variable "smoking history," the value is "1" if smoking history is 10 or greater cigarettes per day, and value is "0" if smoking history is less than 10 cigarettes per day.

*** For the variable "LVH," the value is "1" if left ventricular hypertrophy is found on electrocardiogram (ECG); and value is "0" if there is no left ventricular hypertrophy on ECG, or left ventricular hypertrophy by voltage only criteria.

**** For the variable "diabetes," the value is "1" if the fasting blood glucose is 115 mg/dl or greater, and the value is "0" if the fasting blood glucose is less than 115 mg/dl.