

The VET Registry: Reflecting the Lives of a Generation

Twins have fascinated scientists for centuries as they have tried to determine the extent to which our health and behavior are influenced by our genetic background and our experiences.

Identical, or monozygotic, twins in particular have been studied extensively because they share the same genetic makeup. By looking at how the twins are affected similarly by diseases such as heart disease or differently by their life experiences, such as one twin serving in Vietnam, researchers can draw general conclusions that help to explain and predict health and behavior patterns for us all.

Similarities and Differences

Biomedical research involving adult twins has followed two main approaches. The first, the classical twin study, uses twins to search for evidence of increased frequency of disease within families.

Classical twin studies look for similarity within twins for a particular disease, such as alcoholism. If monozygotic twins are more likely to both

have a disease than dizygotic twins are, this provides evidence that the disease is influenced by genetics.

One of the largest studies involving the Vietnam Era Twin (VET) Registry is a classical twin study of drug abuse conducted by Harvard University. With this type of study, researchers can even estimate the degree to which genetics (sometimes called heritability) and the environment each are involved. The Harvard study, for example, has found that drug abuse, like alcoholism, tends to run in families. The researchers attribute 30 percent of this "clustering in families" to inherited disposition, 30 percent to experiences shared by the twin brothers and 40 percent to environmental influences unique to each twin.

The second type of twin study, the co-twin control study, focuses on identical twin pairs in which one twin's experience is different from the other's. One twin, for example, may exercise regularly, while the other may not. This type of study allows researchers to see how the development of a disease or

WELCOME

For 10 years, participants in the VET Registry have willingly shared the information needed to complete significant research studies that focus on service in Vietnam and look more broadly at health and lifestyle issues. Without this cooperation, the VET Registry would not have become the valuable research tool that it is today. Thank you, everyone, for your willingness to participate!

And welcome to Twin Times, which we hope will continue the exchange of information between us by keeping you up to date on registry activities. Here you'll find briefs that report some of the studies' findings, as well as background about major studies and the VET Registry itself.

Take a look, and see what you have helped to accomplish by being a participant in the VET Registry.

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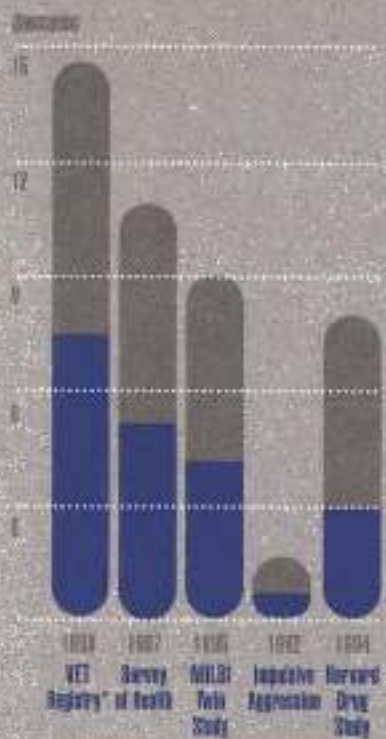
News for Participants

in the Vietnam Era

Twin Registry

Volume 1, 1996

Major Studies Using the VET Registry and Their Dates of Completion



Legend:
 ■ TOTAL NUMBER OF TWIN PAIRS PARTICIPATING
 ■ TOTAL NUMBER OF INDIVIDUAL TWINS PARTICIPATING

*The process of identifying and verifying the twins in the registry took from 1983 to 1986.

symptom may be influenced by a specific experience or activity, such as lack of regular exercise.

One of the most important uses of the VET Registry has been to use the co-twin control approach to examine the health of pairs where one twin served in Vietnam and the other did not.

Looking for Twins

Twins are considerably more prevalent than most people expect. They occur at a rate of about 12 per every 1,000 births, so on average, twins make up about 1.2 percent of the world's population. The rate of twin births varies around the globe. For example, countries in sub-Saharan Africa, like Nigeria, have the highest rate of twin births, while countries in Asia, like China, have the lowest rate. With the increased use of fertility drugs, the number of twin births is on the rise in the United States and other developed countries.

People don't realize how common twins are because twins are only recognized when both members of the pair are together. We see twins together as children at play and at school, but once twins become adults, they are seen together much less frequently.

One of the biggest problems in conducting biomedical studies of adult twins is the lack of readily available and scientifically valid large samples of twins. Without samples of twins that number in the thousands, most chronic diseases are difficult to study.

While all states maintain birth registries that identify twins, there is no way to follow the health of the twins through childhood and adulthood. In contrast, Sweden and Norway have maintained large population-based twin registries of adults for half a century. These registries have been a treasure trove for scientific research on chronic ailments such as cancer and heart disease.

Only two nationwide twin registries exist in the United States—the National Research Council (NRC) World War II Twin Registry and the VET Registry. The NRC WW-II Twin Registry originally contained 16,000 male twins born between 1915 and 1927, all of whom served in the military during World War II. All surviving pairs from this registry are more than 65 years old, so current research focuses on diseases of the elderly, such as Alzheimer's disease and Parkinson's disease.

Building the Registry

The VET Registry contains 7,400 male twin pairs who were born between 1939 and 1957 and who served in the military from 1965 to 1975. Most of the twins in the registry were found through a computerized list of six million veterans obtained from the Department of Defense.

Researchers used computer record linkage methods to select pairs of records of servicemen who were likely to be twins. The matching process linked records based on same last name, different

first name, same date of birth and similar Social Security numbers. The researchers reviewed thousands of hard-copy military records to verify that both members of each pair had the same set of parents.

The process of identifying and verifying the twins in the registry began in 1983 and was not completed until 1986. Since then, ten biomedical studies have been approved and funded. Five of these are completed, and five are ongoing. Many of the initial studies involved mail surveys and telephone interviews. More recently, selected twin pairs have participated in formal psychological testing. (The graph on this page provides a timeline for the major studies.)

Major Studies

The Survey of Health in 1987 was linked to the registry's creation. This was the largest study to date, involving mail and telephone interviews with more than 10,000 participants. The purpose of the survey was to see how military service and exposure to combat related to veterans' long-term health.

The second major study, also a mail and telephone survey, was conducted in 1990 in collaboration with the National Heart, Lung and Blood Institute. The survey sought to identify early cases of cardiovascular disease and to collect information on risk factors for major chronic diseases of middle age, such as hypertension and diabetes.

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What specifically have researchers discovered through studies that use information provided by VET Registry twins? The following briefs highlight some of the findings related to service in Vietnam and to broader health and lifestyle concerns. These briefs also point to areas of ongoing and future research for the VET Registry.

Impact of Vietnam Service on Health Problems

Many veterans worry about whether service in Vietnam has affected their long-term health. Researchers used the VET Registry to investigate this issue by studying data collected in 1987 on 13 categories of self-reported health problems.

Overall, findings show that the self-reported health of Vietnam veterans is generally similar to that of veterans who did not serve in Vietnam. Researchers found no increase among Vietnam veterans for health conditions such as heart problems, high blood pressure, diabetes, stroke, stomach disorders, liver problems and respiratory conditions, joint disorders, urinary conditions, blood disorders and cancer.

However, Vietnam veterans are twice as likely to report hearing problems and

skin disorders as their twin brothers who did not serve in Vietnam. Twins who experienced heavy combat in Vietnam were three times as likely to report skin disorders and hearing problems, which may be due to exposure to explosives.

Nearly 15 years after the end of the Vietnam War, this study also indicated a substantially increased prevalence of post-traumatic stress disorder among veterans who served in Southeast Asia.

The Vietnam War and Later Sleep Problems

A good night's sleep doesn't come easily for many Americans who have problems falling asleep or wake up frequently during the night. Scientists do not know what causes many of these problems. But responses on sleep problems from VET Registry twins are providing the basis for a new study that may advance our understanding of insomnia.

In collaboration with the National Heart, Lung and Blood Institute, researchers have analyzed the genetic effects and role of combat exposure on sleep problems. Results indicate that both genetic disposition and combat contribute to sleep problems. Interestingly, genes seem to play a more important role than combat in determining insomnia.

Adjusting to Life after Service in Vietnam

Vietnam veterans sometimes question whether their service in Southeast Asia had an adverse effect on their marriages, education, occupational success and income. Researchers have examined data collected in 1987 through the VET Registry to study this issue.

Results show that service in Vietnam did not dramatically alter several life experiences for veterans. For example, among identical twin pairs where one brother served in Vietnam and one did not, researchers found no differences in divorce rates, employment status, education or income. These results suggest that most veterans have successfully reintegrated into civilian life after service in Vietnam.

Cigarette Smoking Related to Combat Stress

Are Vietnam veterans who experienced intense levels of combat more likely to be heavy cigarette smokers than veterans with little or no combat experience? To answer this question, researchers used

Monozygotic vs. Dizygotic

Twins typically describe themselves as identical or fraternal. Scientifically, identical twins are referred to as monozygotic, and fraternal twins are referred to as dizygotic. All this means is that monozygotic twins are derived from a single egg fertilized by a single sperm, while dizygotic twins are produced from two eggs fertilized by two separate sperm.

Monozygotic twins share 100 percent of their genetic material, and dizygotic twins share 50 percent of their genetic material, on average. Further, all monozygotic twins must be of the same sex, while dizygotic twins can be the same or opposite sex.

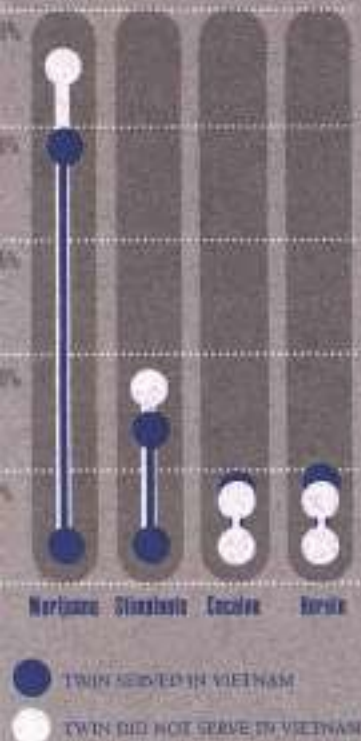
For research involving twins, scientists must carefully assess whether twins are monozygotic or dizygotic. Ideally, this is done by obtaining samples of genetic material (DNA) and comparing them. If the DNA is identical for both twins, they are monozygotic. If not, they are dizygotic.

With large samples of twins, like the VET Registry, DNA testing is impossible. As an alternative, scientists ask adult twins questions about their similarity as children. These questions have been found to be nearly as accurate as DNA testing for classifying twins.

You may recall that one of the first questions you were asked when you joined the VET Registry was, "When you were children, were you alike as two peas in a pod or of ordinary family resemblance?" Researchers all over the world have used this question to help distinguish monozygotic from dizygotic twins.

Vietnam Service and Illegal Drug Use

Percentage of Twins Regularly Using:



Twins who served in Vietnam do not appear to have had a higher instance of regular use of illegal drugs, except for heroin. An analysis of the past history of regular drug use found few differences in drug use, but a history of heroin use was more common among the twin who served in Vietnam compared with his identical twin who did not serve in Vietnam.

the VET Registry to measure cigarette smoking and combat experiences 15 years after veterans were discharged from the military.

An analysis of identical twins that controlled for alcohol consumption and socioeconomic variables found no significant relationship between current cigarette consumption and the level of combat exposure. Responses to the questions, "Have you ever smoked?" "Do you smoke now?" and "Do you smoke more than 29 cigarettes a day?" were not associated with high levels of combat exposure nor with lesser levels of combat or service in Vietnam alone.

Post-Traumatic Stress Disorder and Heredity

Most symptoms of post-traumatic stress disorder (PTSD) are influenced by genetics, researchers reported in a paper published in April 1993 in the *Archives of General Psychiatry*. This study of 4,042 identical and fraternal twins found that some people may be predisposed genetically to developing PTSD.

This helps explain why some veterans who experience extreme trauma never

develop PTSD, while others who experience the same or lesser trauma do suffer from this psychological illness.

Are Anger and Aggression Linked to Genes?

We all experience frustration and stress in our daily lives. However, some people are more likely to become aggressive and irritable as stress builds up. Using data collected from VET Registry twins, researchers have looked at why some people become angry more quickly than others.

Identical twins gave very similar answers to questions about irritability and aggression, researchers found, while fraternal twins gave less similar responses to the same questions. This suggests that an inherited component may influence anger and aggression.

Genes and the Decision to Exercise Regularly

The importance of exercise in maintaining good health has been reported widely. But while some people exercise regularly, others avoid exercise whenever they can. What makes the difference?

Scientists at the National Heart, Lung and Blood

Institute recently used data collected from VET Registry twins to examine why people exercise. They studied two types of exercise—moderate activities, such as walking and stair climbing, and intense exercise, such as jogging, swimming or biking.

Researchers found that the levels of moderate and intense exercise were very similar in twins during adulthood, which suggests that the way we exercise runs in families. In addition, identical twins' intense exercise patterns were more similar than those of fraternal twins, indicating a genetic influence on exercise. The researchers plan next to study the role of exercise on the risk of developing heart disease.

Vulnerability to Drug Use: Genes and the Environment

During the past decade, scientists have shown that alcohol abuse often runs in families and may be due, in part, to genetic factors. An important but unexplored scientific question is whether other drug abuse follows a similar pattern. Researchers now have an answer to this question based on telephone interviews about lifetime drug use with 3,000 VET Registry twin pairs.

The researchers found that illicit drug abuse tends to cluster in families. About 30 percent of the clustering in families can be attributed to inherited predisposition, 30 percent to experiences shared by twin brothers and 40 percent to environmental influences unique to individual twins. Ongoing research is examining whether these influences are the same for different types of drugs, such as cocaine, marijuana, amphetamines and LSD.

Twins and Behaviors Related to Drug Abuse

Many behavioral and emotional problems are associated with drug abuse, scientists have found. In response to an extensive telephone interview in 1992-93, researchers collected data regarding VET Registry twins' lifetime experience with major depression and substance abuse. Results showed that major depression is associated with the abuse of marijuana, amphetamines and cocaine—and tended to occur before the onset of substance abuse among these veterans.

Responses from the same telephone interview allowed researchers to investigate

childhood problems associated with substance abuse. One finding was that conduct disorder—a childhood behavior problem characterized by stealing, lying and excessive fighting—is influenced by some of the same family environmental factors that contribute to marijuana abuse. Yet conduct disorder and marijuana abuse appear to have different inherited components. In another study, adult antisocial behaviors were found to be primarily associated with cocaine abuse and only slightly related to marijuana abuse.

Use of data from the VET Registry is providing invaluable opportunities to examine drug abuse and related behavior and emotional problems. These findings should provide health professionals with a better understanding of substance abuse and mental illness.

Effects of Smoking and Drinking on Weight

Are cigarette smokers thinner than non-smokers? Do people who drink alcohol regularly weigh more than teetotalers? Data from the VET Registry's 1987 Survey of Health were used to examine how cigarette smoking and alcohol consumption influence body weight. This

study, published in the *Archives of Internal Medicine*, focused on identical twins where one twin smoked cigarettes and his brother did not.

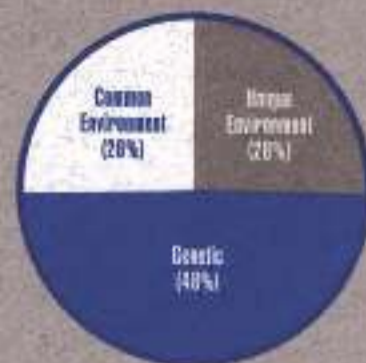
Results indicated that cigarette smokers consistently weighed less than non-smokers—on average, by 7.04 pounds. And former smokers were more likely to be obese (more than 20 percent over ideal weight) than their non-smoking twins. However, alcohol drinking had no impact on weight, even when one twin drank more than two drinks a day and his brother abstained.

The researchers caution against using cigarette smoking to control weight and suggest that programs to stop smoking include a weight management component.

Do Genes Affect the Way We Seek Medical Care?

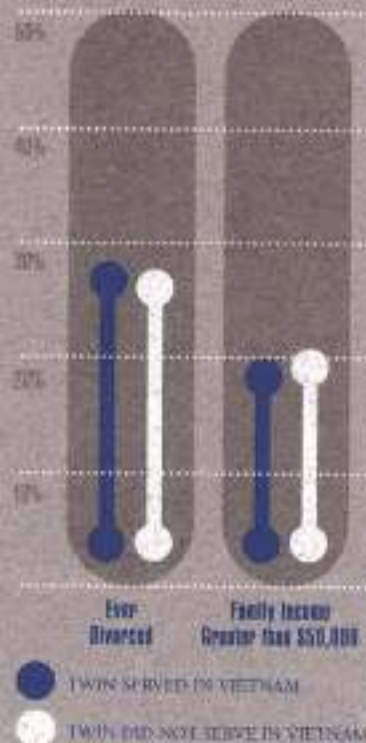
Why are some people more likely to seek medical care than others? This is a question that scientists have tried to answer for decades. Clearly, some factors—illness and health status, location, insurance, income, race and education—play an important role, and behavioral and psychological factors are involved.

The Effect of Genetics on Regular Marijuana Use



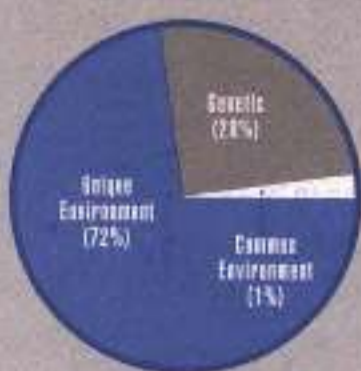
Genetic effects contributed more strongly to a regular pattern of marijuana use than either environmental influences experienced in common by both twins or unique aspects of each twin's environment, according to an analysis of twins' lifetime history of regular marijuana use.

Vietnam Service, Divorce and Income



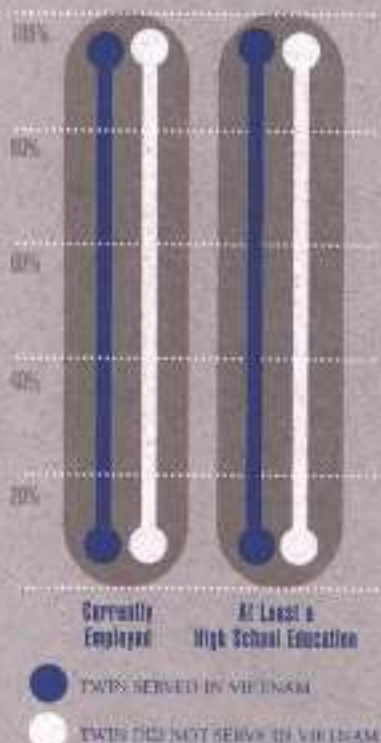
Researchers found little difference in the divorce rate or family income level for pairs of identical twins where one had served in combat and the other had not.

Sleep Problems and Heredity



Unique aspects of each twin's environment account for most of the variability in sleep problems. However, a little more than a quarter of all sleep problems experienced by VET Registry members are due to genetic influences.

Vietnam Service, Employment and Education



An analysis of identical twins showed little difference in employment or educational level where one twin had served in combat and the other had not.

Recently, researchers used data from the VET Registry to explore whether a genetic effect may influence whether a person seeks medical care. Results of the classical twin study suggest that the decision to seek medical treatment for some conditions—such as hypertension, mental disease and hearing problems—may indeed be at least partially influenced by our genes.

The researchers found that the genetic effects related to obtaining medical care vary according to different physical and psychological health conditions. For example, data from the VET Registry confirm that seeking treatment for alcoholism is a genetically influenced trait. More than 40 percent of the likelihood of seeking treatment for alcoholism may be due to a separate set of genetic factors.

The Nature of Gambling Behavior

Once restricted to Las Vegas and Atlantic City, the legal gambling industry has spread across the United States through state-run lotteries and land or water-based casinos. Scientists are concerned that this increase in legalized gambling may also lead to an increase in addictive gambling.

While collecting data on alcohol and illicit drug use

from the VET Registry, researchers also obtained and examined data on addictive gambling for evidence that this behavior may be influenced by genes.

The results show that genes are indeed related to gambling. Genetic effects account for more than one-third of frequent gambling (25 times or more in a year). Beyond that, more than half of all cases of lifetime addictive gambling may be due to genetic effects. These findings match the genetic influence found for other addictive behaviors involving psychoactive drugs.

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Want to Read More? Check Out These Articles

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Registry Q&A

Q: How do scientists gain access to participants in the VET Registry and data already collected about them?

A: Investigators are only allowed access to the VET Registry for a few outstanding research projects. Granting access is an extremely selective task that takes two to four years.

The process begins with the submission of a detailed description (often 60 pages or more) of the proposed research project to a granting organization such as a private foundation or government body like the National Institutes of Health. The VET Registry itself does not fund research projects because they often cost hundreds of thousands of dollars.

Although human studies committees from the researcher's institution and the granting agency must approve the safety of the project for human participants, access to the VET Registry is not granted until the proposal is accepted by the registry's own Human Studies and Scientific Advisory Committees. The Human Studies Committee makes sure that the project presents little or no risk to registry members. The Scientific Advisory Committee, a group of inter-

nationally renowned investigators, reviews the proposal's technical merit and ensures that it will make an important contribution to science.

Investigators interested in gaining access to the VET Registry should call (708) 345-4400.

Q: What steps does the VET Registry take to make sure that personal and sensitive information about participating twins is kept confidential?

A: All information that VET Registry members provide, such as answers to a survey, is strictly confidential. Although scientists analyze information from Registry research projects, NO identifying information is ever released to them. In fact, a registry member must provide specific written approval for his name and other identifying material to be released.

Only two people have the key to link registry data with an individual. They are William Henderson, Ph.D., the registry's director, and Mary Ellen Vitek, the registry's coordinator. In addition to the registry's own maintenance of confidentiality, some sensitive research projects are further protected by a certificate of confidentiality issued by the federal government. The certificate prevents court or governmental agencies from examining answers collected as part of the research project.

Who's Who at the VET Registry

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This newsletter is published by the Vietnam Era Twin Registry to provide participants with up-to-date information about activities and research related to the VET Registry. To obtain additional copies or for more information about Twin Times or the VET Registry, contact Mary Ellen Vitek, registry coordinator and newsletter editor, at (708) 345-4400.

Special thanks to Jeff Scherrer, St. Louis VAMC, and Dr. Jack Goldberg for their contributions to this first issue.

COVER STORY

The VET Registry

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A smaller mail and telephone interview study in 1992 sought to determine the genetic correlates of hostility and aggression.

In 1994, researchers used an extensive structured telephone interview to collect information as part of the Harvard Twin Study on Substance Abuse. The study has focused on understanding the genetic and non-genetic factors that may influence the use and abuse of alcohol and illegal drugs.

Two of the ongoing substance abuse studies involve telephone interviews (alcohol

abuse and health services utilization, and a twin-family study of alcoholism).

Three others (consequences of drug abuse, vulnerability to alcohol abuse, and the twin study of post-traumatic stress disorder) involve the detailed in-person

psychological testing of a few hundred selected twins.

Many of these twins are asked to travel at the investigator's expense to Boston, St. Louis or Davis, Calif., to participate in a day of testing.

Keep Us Informed

The VET Registry staff would like to keep all participants informed about registry activities, new research findings and future projects. To do so, we encourage you to notify us of any changes in your address or telephone number:

NAME _____

ADDRESS _____

CITY _____

STATE _____

ZIP _____

HOME PHONE _____

WORK PHONE _____

Return this form to Mary Ellen Vitek, VET Registry Coordinator, CCSHS, P.O. Box 1389, Hines, IL 60141. Thank you!

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FORWARDING AND ADDRESS CORRECTION REQUESTED