

Newsletter Glossary

Discordant: This refers to differences within a pair of twins. A twin pair "discordant for combat exposure" would be a pair where one brother was exposed to combat and the other brother was not.

Magnetic resonance imaging (MRI): Produces detailed 3-dimensional pictures of the inside of the human body. Researchers use MRI to show the size, appearance, and form of tissues and organs in the body. Functional MRI (fMRI) is a special type of MRI used to see how brain cells work.

Methylation: A type of chemical modification of DNA that can be inherited, but also changes during your life without changing the original DNA sequence. The modification can alter how your genes work during the course of your life. DNA methylation happens naturally over time and helps determine which genes get switched "on and off" as we age.

Positron emission tomography (PET): Produces 3-dimensional pictures of the inside of the human body. Researchers use PET imaging to see biologic processes that occur within tissues and organs in the body.

Post-Traumatic Stress Disorder (PTSD): A psychiatric diagnosis caused by a traumatic event. PTSD can develop after experiencing or witnessing an event that causes intense fear, helplessness, or horror.

Researcher Spotlight: Drs. William Kremen and Michael Lyons

We would like to introduce Drs. William Kremen and Michael Lyons, both of whom are principal investigators of the Vietnam Era Twin Study of Aging (VETSA). VETSA is a VET Registry longitudinal study supported by grants from the National Institute of Aging. The VETSA study is located in both San Diego, CA and Boston, MA.

VETSA's goal is to follow twins throughout their lives, contacting them every 5 years to learn about genetic (nature) and environmental (nurture)



Registry twins, and follow-up research on these twins is currently underway. Over 1,000 twins have already participated in the ongoing VETSA 2 follow-up, and plans are being made for the VETSA 3 follow-up. This project has resulted in over 50 published articles in the scientific literature, including a March 2012 article in *Science*, one of the world's top scientific journals.

Dr. Kremen is a Professor in the Department of Psychiatry at the University of California, San Diego. He is the Director of the Twin Research Laboratory in the department's Center for Behavioral Genomics. He is also Chief of the Lifespan Unit in the Center of Excellence for Stress and Mental Health at the VA San Diego Health Care System.

factors that influence the aging process. The VETSA magnetic resonance imaging (MRI) studies are linked to the main VETSA project, and focus on the brain and how it changes as people age.

Through the VETSA studies, Drs. Kremen and Lyons hope to learn about the influence genes have on the aging brain. The VETSA studies include over 1,200 VET

Dr. Kremen's research focuses on the behavior genetics of cognitive and brain

(Continued on page 6)

Drs. William Kremen (left) and Michael Lyons (right)

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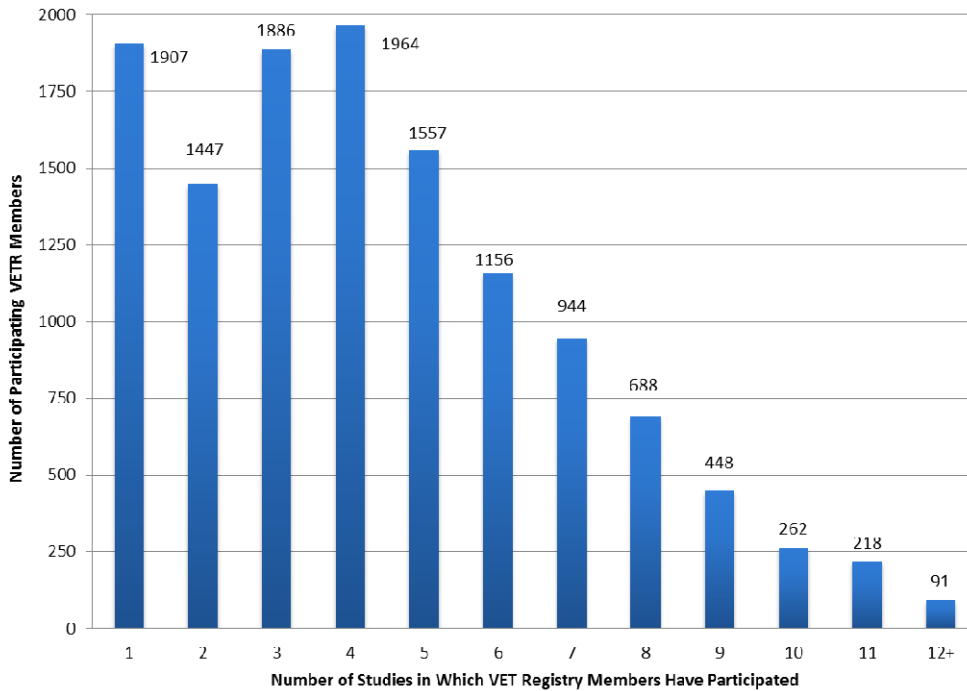


Seattle Epidemiologic
Research and
Information Center

VET Registry Twins

VET Registry Member Study Participation

Figure 1. VETR Members and Studies Participated In



Note: This figure excludes the 2261 VETR Members who have not participated in any studies.

Many VET Registry members have participated in more than one Registry study. This graph displays the number of VET Registry members who have participated in a given number of studies – for example, 1,886 Registry members have each participated in 3 studies. On average, Registry members who have participated in research have participated in between 3-4 studies, and approximately 36% of these members have participated in 5 or more studies.

The VET Registry Staff would also like to thank each and every one of our members for their ongoing support and participation in our research studies. Without you the VET Registry would not exist, and we look forward to many more years of collaboration!

Updated Facts on Twins

1 in every 30 babies born in the United States was a twin in 2009, compared to 1 in 53 in 1980.

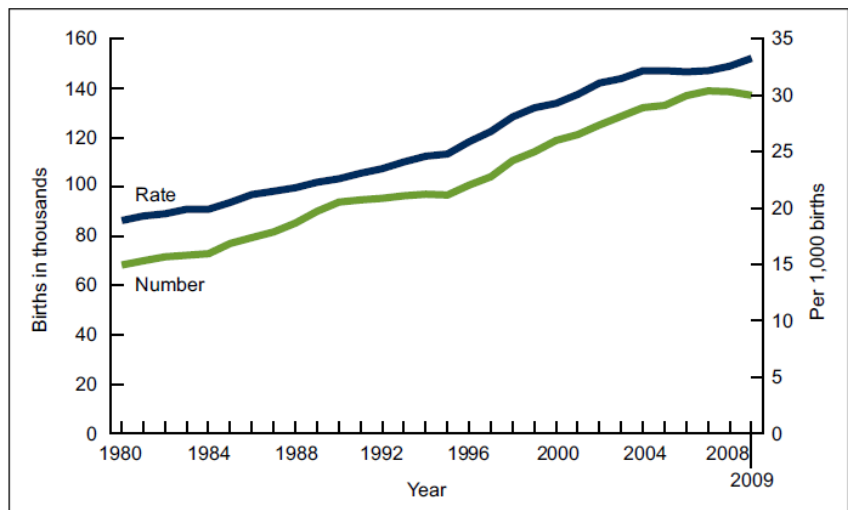
Twinning rates increased for women of all age groups, but was largest in women aged 30 and over. Though in 2009 women tended to be older at childbirth than in 1980, this increased maternal age only accounts for about one-third of the rise in twinning rates over time. The rise in twinning not accounted for by older maternal age is likely associated with the use of infertility treatments, which became more prevalent during the 1980s and 1990s.

If the twin birth rate had not changed, approximately 865,000 fewer twins would have been born in the United States in the last three decades.

Source: CDC/NCHS, National Vital Statistics System, January 2012

One in every 30 infants born in 2009 was a twin.

Figure 2. Number and rate of twin births: United States, 1980-2009



SOURCE: CDC/NCHS, National Vital Statistics System.

Tips for Healthy Living

Eat 5, Move 10, Sleep 8

One of the best ways to make sure you are living a healthy life is by focusing on heart health. Health professionals from the Mayo Clinic have developed a quick-start plan for heart health, called **Eat 5, Move 10, Sleep 8**. This two-week program is a quick, simple way to start making the small lifestyle changes that can have a big impact on your heart health. The tips included in the Eat 5, Move 10, Sleep 8 plan are meant to be tried for two weeks before you move on to a more established healthy heart program, when you might consider trying other reputable diet and exercise routines. The purpose of Eat 5, Move 10, Sleep 8 is to help you get started with something and keep at it.

Try it out!

Eat 5

Concentrate on eating at least five servings of fruits and vegetables per day to boost your heart health. Consider starting by snacking on fruits or vegetables throughout the day, or trying to work them in to your day-to-day meals. When you're just starting out, don't worry so much about what you shouldn't eat, focus more on getting five (or more!) servings of fruits and vegetables per day.

Move 10

Add at least 10 minutes of moderately intense physical activity to what you do every day. Research suggests that 60 to 90 minutes of physical activity per week can reduce your heart disease risk by up to half. That's just about ten minutes of exercise per day – a big benefit for a small commitment! As you become more active, you can try to increase your total exercise time per day.

Sleep 8

Try to get eight hours of good, quality sleep each night, as quality sleep is beneficial for your heart. Each person's sleep needs vary, but eight hours per night is a good target to strive for.

Source: The Mayo Clinic, January 2012

Information to Help You Stay Well

Scientists estimate that about one-third of the most common types of cancer could be prevented by making lifestyle and dietary changes. The American Cancer Society suggests a few ways to reduce your cancer risk:

- Avoid using tobacco products
- Maintain a healthy weight
- Get moving with regular physical activity
- Eat healthily, with plenty of fruits and vegetables
- Limit how much alcohol you drink
- Protect your skin when you're in the sun
- Know yourself, your family health history, and your health risks
- Have regular check-ups with your doctor and cancer screening tests

Regular check-ups and screenings from your doctor for various types of cancers are important, as they can increase your chances of detecting cancer early, when treatment is most likely to be successful. For example, the American Cancer Society recommends that both men and women begin a screening schedule for colorectal cancer at age 50. Consider talking to your doctor about the pros and cons of various cancer screenings, as well as the types of testing involved, so you can make the right cancer screening schedule for you.

For more tips on how to reduce cancer risks or to learn more about cancer, you may visit the American Cancer Society online at www.cancer.org, or the American Institute for Cancer Research, at www.aicr.org.

Source: American Institute for Cancer Research, American Cancer Society, June 2012

VET Registry Study Updates

RECENTLY COMPLETED STUDY:

★Memory and Hippocampus in Vietnam-era Twins with Post Traumatic Stress Disorder

Principal Investigator: Dr. J. Douglas Bremner, Emory University, GA

The purpose of this study is to look at an area of the brain involved in learning and memory (called the hippocampus) over time and see how that relates to twins who were exposed to combat and have a diagnosis of PTSD. The study includes an in-depth clinical evaluation involving interviews, paper and pencil questionnaires, tests of memory, laboratory testing, magnetic resonance imaging (MRI), and positron emission tomography (PET) imaging of the brain. This study was completed in late 2011 with 53 participants.

CURRENT ONGOING STUDIES:

★Veteran Health Study

Principal Investigators: Dr. Jack Goldberg, VA Puget Sound, Seattle VA and Dr. Kathy Magruder, Charleston VA, Charleston, SC

The goal of the Veteran Health Study is to better understand the physical and mental health of Vietnam-era Veterans as they grow older. Thousands of twins from the VET Registry have already participated in the Veteran Health Study and all VET Registry twins will be asked to participate. In this study participants complete a pencil and paper questionnaire about their health and are then interviewed by telephone about their mental health. The knowledge gained from this study will help researchers understand how aging affects PTSD

and related conditions. This information will assist the VA in designing programs for prevention and treatment of the health and mental health problems of aging Veterans. This study has recruited 8,097 twins so far.

★Twins Heart Study 2 (THS-2)

Principal Investigator: Dr. Viola Vaccarino, Emory University, GA

The goal of this research is to assess the influence of psychosocial stressors on cardiovascular disease. The THS-2 study is a follow-up of twin pairs with PTSD or major depression who were participants in one of our previous studies. We use objective cardiovascular measures, such as ultrasound and positron emission tomography (PET) imaging of the heart. All participants travel to Atlanta to undergo testing. So far, this study has recruited 137 participants.

★Common Genetic Pathways Linking Depression to Cardiovascular Disease: A Twin Study

Principal Investigator: Dr. Jinying Zhao, University of Oklahoma Health Science Center, Oklahoma City, OK

The goal of this study is to identify genetic and epigenetic factors that are associated with depression, cardiovascular disease, or both. Genetic differences in about 500 genes are being studied through secondary analysis. This study also measures DNA methylation levels in specific genes and tests their associations with depression or cardiovascular disease. This study recently began analysis on data from Dr. Viola Vaccarino.

★Decelerated Biological Aging as a Potential Mechanism for the Cardioprotective Effects of the Mediterranean Diet on Cardiovascular Disease: A Twin Study

Principal Investigator: Dr. Silvia Eufinger, Emory University, GA

The goal of this study is to systematically examine decelerated biological aging as a potential mechanism linking the Mediterranean diet to its cardioprotective effects. The study assesses the association between markers of biological aging and adherence to the Mediterranean diet. This study opens a new and important line of investigation, examining how adherence to a healthy diet could decrease the speed of biological aging and prevent cardiovascular disease. This study recently began secondary analysis on data from Dr. Viola Vaccarino.

★Epigenetics, a Potential Mechanism Linking Depression to Cardiovascular Disease

Principal Investigator: Dr. Shaoyong Su, Georgia Health Sciences University, GA

The main objective of this project is to explore the potential mechanisms linking depression to cardiovascular disease. Specifically, this study plans to identify the DNA methylation changes between depressed twins and their non-depressed co-twin. This study uses DNA methylation testing and identifies the sites on the gene where methylation levels differ between depressed twins and their non-depressed co-twin. This will help clarify the possible role of methylation level changes in the develop-

VET Registry Study Updates

ment of atherosclerosis (hardening of the arteries). This study has recently begun secondary data analysis on data from Dr. Viola Vaccarino.

★Twin Study of Biological Markers for Post Traumatic Stress Disorder (PTSD)

Principal Investigators: Dr. Lisa Shin and Dr. Roger Pitman, Harvard School of Medicine, Boston, MA

This study is using functional magnetic resonance imaging (fMRI) to examine the brain function in identical twin pairs, where only one twin was exposed to combat during the Vietnam War. The goal of this study is to determine if specific brain regions function differently in combat Veterans with PTSD compared with their identical twins who were exposed to combat and do not have PTSD. This study has recruited 34 participants thus far.

★The Genetics of Posttraumatic Psychopathology

Principal Investigator: Dr. Erika J. Wolf, Boston University, MA

This research focuses on evaluating how exposure to combat affects the genetic and environmental risk for psychopathology. This study uses sophisticated data analytic techniques to model common mental disorders spanning the internalizing (anxiety and mood disorders) and externalizing (antisocial personality disorder and substance use disorders) dimensions. Preliminary work suggests that combat exposure may alter the genetic risk for these kinds of symptoms and disorders. This study began analysis on data from the VET Registry.

★Family Studies of Health and Behavior

Principal Investigators: Dr. Theodore Jacob, Palo Alto VA, Palo Alto, CA, and Dr. Kathleen Bucholz, Washington University, St. Louis, MO

Studies at the VA in Palo Alto, CA focus on the mental and physical health of Veterans and their families with an interest in determining how genes and experiences affect smoking, drinking, drug use, and depression. In one study, twins are being followed throughout their adult years to determine how their drinking habits change as they age. Another study focuses on adult children of twins to determine similarities and differences in health patterns across the generations. It is hoped these studies will help clinicians design prevention and treatment programs. Recruitment for this study began in mid-June,

At Washington University in St. Louis, MO, the Transition to Adulthood Project (TAP) began collecting data from Registry twin fathers and their families in 2002 and is currently conducting follow-up interviews with the adult children of twins. The TAP team is measuring young adult milestones, like marriage and parenthood, completion of education, occupation, and job satisfaction. The team will examine how these milestones relate to health, especially in the areas of mood and the use of alcohol, tobacco and drugs. The most recent wave of interviews for TAP finished in May 2012 and interviewed 106 adult children.

★Biopsychosocial Approaches to Healthy Aging

Principal Investigator: Dr. Terrie Vasilopoulos, University of Chicago

The goal of this study is to understand aging by examining the complex relationships among cognitive, physical and psychosocial function. The objective of this study is to determine whether physical function (e.g. lung function, blood pressure) and psychosocial factors (e.g. self-esteem, socioeconomic status) influence the genetic and environmental influences underlying cognition. This study recently began analysis using data from Drs. William Kremen and Michael Lyons.

★Genetic and Epigenetic Factors of Age-Related Cognitive Decline: A Twin Study

Principal Investigator: Brinda Rana, PhD, University of California, San Diego

The goal of this study is to better understand genomic and environmental predictors of age-related neurocognitive changes through epigenetic studies. Although DNA methylation patterns are inherited, they can also be highly influenced by the environment. The study will examine what factors may cause changes in DNA methylation throughout the life course, and how those changes may influence the process of aging, as well as age-related cognitive decline. DNA samples are currently being collected on wave 2 VETSA participants, and will be compared to previous data collected by Drs. William Kremen and Michael Lyons.

VET Registry Research

(**Researcher Spotlight Article**, continued from page 1)

aging – that is, he studies the genetic and environmental influences that make for successful aging, or age-related declines. He is also the Principal Investigator of the VETSA Longitudinal MRI Twin Study of Aging, an associated study that involves brain imaging of many of the VETSA participants.

Dr. Lyons, who is a Vietnam Veteran, has worked with the VET Registry since the late 1980s. He is a Professor and Chairman of the Psychology Department at Boston University. He is also a fellow and officer of the American Psychopathological Association and is Chief of Twin Research at the Harvard Institute of Psychiatric Epidemiology and Genetics. Dr. Lyons' general interests are in psychiatric epidemiology and behavioral and psychiatric genetics and his research focuses on genetic influences on aging and psychopathology.

Drs. Kremen and Lyons have authored over 120 and 175 articles, respectively, in scientific journals, and many of these articles describe research with the members of the VET Registry. Some of these articles are detailed in the "Select VET Registry Research Publications" list in this newsletter.

Select VET Registry Research Publications

Zhao J, Goldberg J, Bremner JD, Vaccarino V. Global DNA methylation is associated with insulin resistance: a monozygotic twin study. *Diabetes*, 2012, 61(2), 542-546.

Zhao J, Goldberg J, Vaccarino V. Promoter methylation of serotonin transporter gene is associated with obesity measures: a monozygotic twin study. *International Journal of Obesity (London)*, Advance online publication, 2012 Jan 31.

Su S, Votaw J, Faber T, Khan D, Bremner JD, Goldberg J, Nichols K, Van Tosh A, Vaccarino V. Measurement of heritability of myocardial blood flow by positron emission tomography: the Twins Heart Study. *Heart*, 2012, 98(6), 495-499.

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Kremen W, Panizzon M, Neale M, Fennema-Notestine C, Prom-Wormley E, Eyler L, Stevens A, Franz C, Lyons M, Grant M, Jak A, Jernigan T, Xian H, Fischl B, Thermenos H, Seidman L, Tsuang M, and Dale A. Heritability of brain ventricle size: Converging evidence from inconsistent results. *Neurobiology of Aging*, 2012, 33(1), 1-8.

Kremen W, Koenen K, Afari N, Lyons M. Twin studies of posttraumatic stress disorder: Differentiating vulnerability factors from sequelae. *Neuropharmacology*, 2012, 62(2), 647-653.

Chen C-H, Gutierrez ED, Thompson W, Panizzon M, Jernigan T, Eyler L, Fennema-Notestine C, Jak A, Neale M, Franz C, Lyons M, Grant M, Fischl B, Seidman L, Tsuang M, Kremen W, Dale A. Hierarchical genetic organization of human cortical surface area. *Science*, 2012, 335(6076), 1634-1636.

Shin LM, Bush G, Milad MR, Lasko NB, Brohawn KH, Hughes KC, Macklin ML, Gold AL, Karpf RD, Orr SP, Rauch SL, Pitman RK. Exaggerated activation of dorsal anterior cingulate cortex during cognitive interference: a monozygotic twin study of posttraumatic stress disorder. *American Journal of Psychiatry*, 2011, 168(9), 979-985.

Eufinger SC, Votaw J, Faber T, Ziegler TR, Goldberg J, Bremner JD, Vaccarino V. Habitual dietary sodium intake is inversely associated with coronary flow reserve in middle-aged male twins. *American Journal of Clinical Nutrition*, 2012, 95, 572-579.

Shah AJ, Su S, Veledar E, Bremner JD, Goldstein FC, Lampert R, Goldberg J, Vaccarino V. Is heart rate variability related to cognitive performance in middle-aged men? *Psychosomatic Medicine*, 2011, 73(6), 475-482.

Scherrer JF, Xian H, Pan H, Pergadia ML, Madden PA, Grant JD, Sartor CE, Haber JR, Jacob T, Bucholz KK. Parent, sibling and peer influences on smoking initiation, regular smoking and nicotine dependence. Results from a genetically informative design. *Addictive Behaviors*, 2012, 37(3), 240-247.

VET Registry Staff Introductions

Nicholas L. Smith, PhD, is the Director for the VET Registry and the Seattle ERIC. Dr. Smith provides overall leadership for the administrative and scientific goals of the Registry.

Jack Goldberg, PhD, is an epidemiologist with more than 25 years of experience in the management and analysis of complex epidemiological studies. Dr. Goldberg has intimate and unique knowledge of the VET Registry, having worked at the Registry since 1983.

Alaina Mori, BA, is the VET Registry Program Manager. Ms. Mori manages the overall Registry administration, data management and human subjects' protections. Ms. Mori ensures that the day-to-day operations of the Registry run smoothly. You can contact Ms. Mori toll free at (866) 774-9647 or (206) 277-5126.

Melyssa Tsai, BA, is the VET Registry Research Coordinator for the Veteran Health Study. Ms. Tsai coordinates data security matters for Registry studies and contractors. She also coordinates the biospecimen repository.

Nicole Waiss, BS, is a VET Registry Research Assistant and assists with the coordination of family and in-person studies and in-person assessment studies.

Sarah Shirley, BA, is a VET Registry Research Assistant and assists with coordinating in-person studies and with day-to-day Registry operations.

Seattle ERIC Staff:

Nicholas L. Smith, PhD
ERIC Director

Phil Terry, MHA
Associate Director of Operations

Carrie Gehring, CPS/CAP, BSTM
Administrative Support Specialist

Kathryn Moore, PhD
Research Data Manager

Alexandra Fox, MSIS
Research Data Specialist

Chris Forsberg, MS
Biostatistician

Vickie Blakey, BA
Program Assistant

Jen Sporleder, BS
Quality Assurance Specialist



From left to right: Nicholas L. Smith, Sarah Shirley, Nicole Waiss, Alaina Mori, Melyssa Tsai, and Jack Goldberg

✂

Name: _____

Address: _____


City: _____ State: _____ Zip: _____

Home Phone: _____

Mobile Phone: _____

Work Phone: _____

Email Address: _____



Have you moved? We would like to hear from you!

To update your contact information call 1-866-774-9647 or follow the directions below:

1. Please cut out the change of address form
2. Fill out the form in blue or black ink
3. Place form in an envelope, affix postage, and mail to:
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 Vietnam Era Twin Registry
 1660 South Columbian Way (S-152-E)
 Seattle, WA 98108

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