WASHINGTON STATE  TWIN REGISTRY

Annual Report

Seattle, WA | Spokane, WA

Overview

This report summarizes the major achievements and activities of the Washington State Twin Registry (WSTR) during FY17 (July 2016 – June 2017), and the last four months of FY16 (March 2016 – June 2016), reflecting the period in which an agreement between Washington State University and the University of Washington to establish the WSTR was finalized.

Contents

About the Washington State Twin Registry

In 1998, Dedra Buchwald, a professor of medicine at the University of Washington (UW), lost her wallet containing her driver's license. She went to the Washington State Department of Licensing (DOL) to get a replacement. As she filled out the form, she noticed an interesting question: "Are you a twin or a triplet?" It gave her an idea…

Across the nation, the Washington State DOL is unique for its interest in twins. This interest stems from the way in which the DOL creates identification codes for driver's licenses. Each code is a sequence of letters and numbers based on the applicant's name and birth date. If two or more applicants share the same last name and the same birthday, as do twins and triplets, the DOL would run the risk of issuing the same code to more than one driver. Hence the need to identify twins.

Dr. Buchwald's inspiration was simple and powerful. What if she and the Washington State DOL could work with twins in Washington to create a research registry? No such registry existed in the region. After consulting with her colleague Jack Goldberg, a scientist who developed a twin registry for the United States Department of Veterans Affairs, she contacted the Washington State DOL to set up a meeting.

Drs. Buchwald and Goldberg went to the state capital and laid out their plan to form a twin registry before representatives of the DOL. In 1999, the Washington State Attorney General approved the sharing of contact information between the DOL and the UW (both of which are state institutions). With that the UW Twin Registry was born. The Washington State DOL sends the names and contact information of individuals who indicate they are a twin when applying for or renewing a driver's license or state identification card to the Twin Registry on a weekly basis. The Registry sends letters to these twins inviting them to join the Registry. Thousands of twins have joined the Registry since its establishment, making it an invaluable resource to the research community.

In 2013, Dr. Glen Duncan took over as Director of the UW Twin Registry. We made changes to recruitment to streamline our processes, such as allowing volunteers to join via our web page. Near the end of 2013, we also received approval to begin recruiting twins under 18 to join the Registry, representing an entirely new direction for the Registry.

In the summer of 2015, Dr. Duncan accepted a faculty position with Washington State University (WSU) Spokane. With this change, and recognizing the great potential for the Registry as a unique research resource, leadership at UW and WSU worked together to finalize a transition plan and the WSTR was born. Although our name has changed, our procedures and mission have remained the same. Dr. Duncan and Dr. Elizabeth Blue, a faculty member in UW's School of Medicine and Assistant Director of the Registry, are now working together and committed to making the WSTR an exceptional resource for WSU, the UW, and, more importantly, the State of Washington.

Our Impact

The WSTR has the potential to have a great impact on scientific growth and health-related research – from basic science to public health prevention and intervention efforts. Twins provide a potential resource and research tool for medical and scientific researchers to collaborate and use groundbreaking technologies such as genomic and proteomic tools and environmental geocoding.

Combining twin and molecular methods can dramatically impact public health by advancing fields such as pharmacogenomics, individualized medicine, and disease-specific treatments. Research focused on environmental contributions to disease may lead to better community-based approaches to disease prevention as well as targeted interventions for individuals at highest risk.

Staff

Director: Glen Duncan, PhD

Dr. Duncan's academic training is in physical education (BS, 1992, East Stroudsburg University of Pennsylvania) and exercise physiology (MS, 1994, Ball State University; PhD, 1997, University of Tennessee). Following graduate school, he completed postdoctoral research training (1998-2002) and then joined the faculty at the University of Florida (2002-2003), both in the Department of Medicine, Division of Endocrinology and Metabolism. He joined the Core Faculty of the Nutritional Sciences Program, Department of Epidemiology at the University of Washington in July 2003. In June 2015, he accepted a position as a Professor in the newly established Elson S. Floyd College of Medicine, and Chair of the Nutrition and Exercise Physiology program at Washington State University Spokane, where the WSTR is administratively housed. His major focus is related to macro-level influences (built environment, social environment, policies) on physical activity, nutrition, and chronic disease within an ecological framework.

Assistant Director: Elizabeth Blue, PhD

Dr. Blue studied Economics and Anthropology at Indiana University (BS, 2003), and Anthropology at the University of Utah (MS, 2005; Ph.D., 2008). Her graduate work focused on the principles of evolutionary and population genetics. She pursued training in statistical genetics as a postdoctoral fellow at the University of Washington (2008). She joined the faculty at the University of Washington in the Department of Medicine, Division of Medical Genetics (2011). She has been the chair of the Young Investigators committee of the International Genetic Epidemiology Society since 2013, joined the Statistical Genetics Program faculty in 2014, and the Institute of Public Health Genomics faculty in 2015. Dr. Blue's research focuses on identifying genetic variants influencing complex traits, such as Alzheimer Disease and autism spectrum disorder. Her recent work has delved into the complexities of Mendelian traits as well, including oculocutaneous albinism, familial idiopathic pulmonary fibrosis, and others.

Scientific Operations Manager: Ally Avery, MS

Ms. Avery studied sociology at Western Washington University (BA, 2009) and received her Master of Science in Predictive Analytics from Northwestern University (2016). She has experience with all aspects of twin studies, including grant, budget, and protocol development, building and maintaining study databases, data collection, and data analysis.

Scientific Advisory Board

The WSTR has an advisory board consisting of faculty selected by the Director and Assistant Director, and a pair of twins from the Registry.

Hans P. A. Van Dongen, PhD
Research Professor and Director of the Sleep and Performance Research Center, Washington State University

Naomi Chaytor
Associate Professor, Washington State University

Paul Whitney
Professor, Washington State University

Jack Goldberg
Research Professor of Epidemiology, University of Washington

Nicholas L. Smith, PhD
Professor, University of Washington

Eric Strachan, PhD
Assistant Professor, University of Washington

Eric Turkheimer
Professor, University of Virginia

Brent Lewis and Brian Lewis
WSTR members

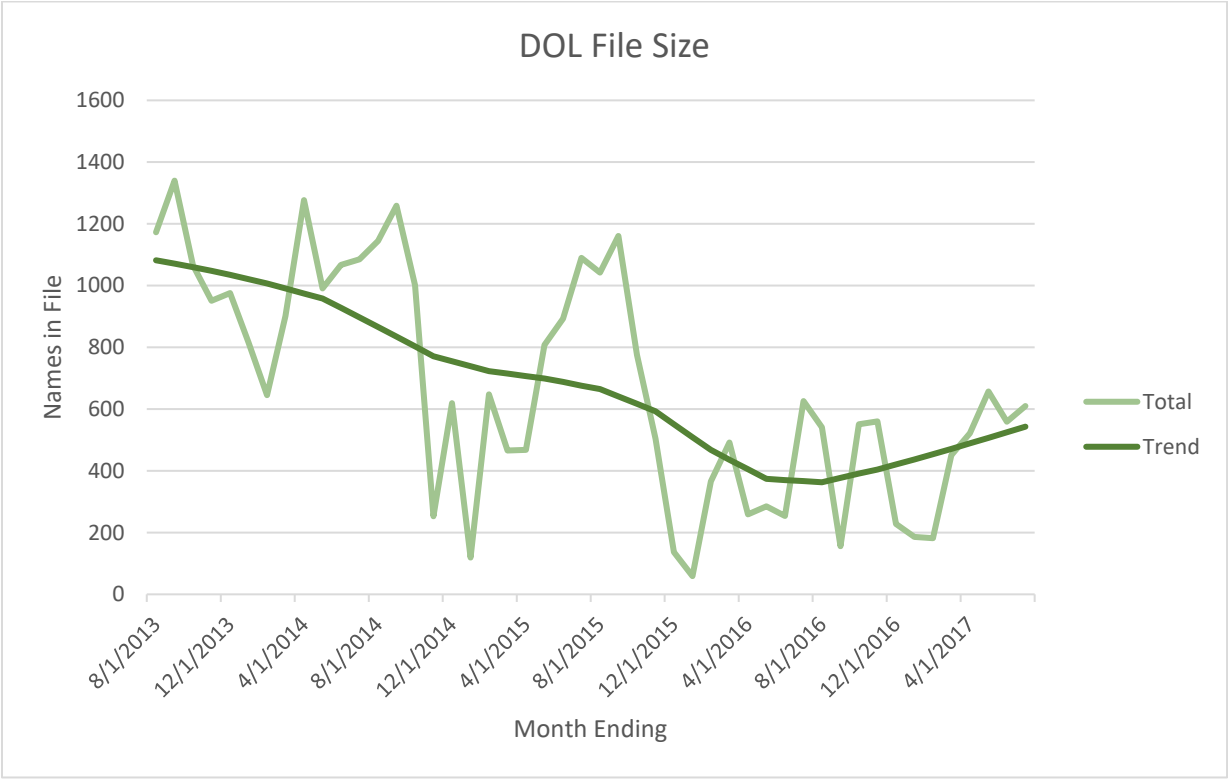
The Registry

The WSTR database contains the contact information for all twins (and their parents, for twins under the age of 12) who have completed an initial enrollment survey. Contact information is updated regularly.

DOL Partnership

As noted previously, the Washington State DOL is unique in that it encodes an individual's last name, first and middle initial, and date of birth in the driver's license or identification card number. Based on this formula, twins have the potential to generate the same license number. To avoid issuing a duplicate license number, the DOL asks all individuals getting a new license or renewing their existing license if they are a twin. The month of birth is coded differently for the second twin. The DOL compiles a list of these names on a weekly basis and forwards them to the Twin Registry. In the past we sent invitations monthly, but our current procedure is to send them out on a quarterly basis. DOL records are also used to update contact information for twins who are already in the Registry and still live in Washington State.

The following graph shows the trend in the number of names we receive from the DOL. In general, the number of names that we receive has been declining, however, it has started to trend upward as of FY17. This increase could reflect the increased rates of twin births since 1980. In 1998, 2% of births in Washington State were twins, and this has steadily increased to 3% as of 2015, the most recent year for which data was available. These individuals are now be at the age where they would be getting a permit and/or license. We will monitor this trend to see if it continues into FY18.



In FY17, we received the names of 6,452 unique individuals:

- 163 individuals were already in the Registry (license renewals)
- Twin pairs and higher order multiple sets are identified by matching last name, date of birth, and/or address.
    - 1,770 individuals were a member of a twin pair, representing 885 complete pairs
        - 285 male-male, 338 female-female, 262 male-female pairs
    - 70 individuals were a member of a triplet or higher order multiple group, and were not eligible for an invitation
        - 22 sets of triplets/higher order multiples

Recruitment

To streamline our processes and reduce waste in printed materials, we have partnered with the WSU Social and Economic Sciences Research Center (SESRC).

SESRC Partnership

The SESRC, located at the WSU Pullman campus, prints materials for mailings on-demand, eliminating the need for storage space for recruitment materials. The SESRC also mails out paper materials at a reduced bulk rate, saving money. Mailed surveys are returned to their offices and entered into a secured database by SESRC staff. Identifiable information is kept in an encrypted database. Once data has been entered, it is securely shared with the WSTR.

Our last major recruitment mailing took place in the spring of 2016. We sent three rounds of invitations by mail. Participants received a link to complete the survey online in the first mailing. If they did not complete the survey after that mailing, they received two additional mailings with a paper version of the survey. The following table summarizes our response rates from this mailing:

	Number in mailing	Mail returned	Removed	Completed survey	Enrolled*
Adult index twins (DOL 18+)	6,321	443 (7.0%)	969 (15.3%)	596 (9.4%)	158 (26.5%)
Adult cotwins (18+)	255	0	0	49 (19.2%)	49 (100%)
Teens (13-17)	1,157	21 (1.8%)	75 (6.5%)	196 (16.9%)	136 (69.4%)
Children (0-12)**	74	6 (8.1%)	3 (4.1%)	9 (12.2%)	9 (100%)

* Percentage of completed surveys

** Surveys are completed for both twins by the parent

Once we receive a survey from an adult respondent, if their cotwin was not in the mailing list, and if they provided their contact information, we send them an invitation to participate. We ask that index twins only provide contact information if their cotwin has agreed to provide it. Invitations are sent in a similar manner to the index twin, except we first send an invitation via email if an email address has been provided. This allows us to follow up and enroll twins in a timely manner.

Because our procedures were changed during the move from UW to WSU, our response rates for cotwins were slightly lower than we would have expected. However, our procedures have now been finalized, so we expect that moving forward our response rates will return to a similar level as we had in the past.

Volunteers

In 2013, we added the ability to enroll twins who did not come through the DOL system. We added survey request pages to our website for both adults and children. The form collects the person's name (or the parent's name for children under 12), the name of the cotwin, the date of birth, and how they heard about our Registry. The following table summarizes our volunteer referral sources as of 6/30/17.

How did you hear about the Registry?

Source	Percent
Department of Licensing	14.9
Facebook	9.1
Friend/Relative	22.7
Multiples group	2.6
My twin received an invitation	2.6
Website	32.5
Other	14.3

We send volunteer invitations by email, unless a mailed invitation is requested. However, the procedure for inviting cotwins of volunteers is the same.

Membership

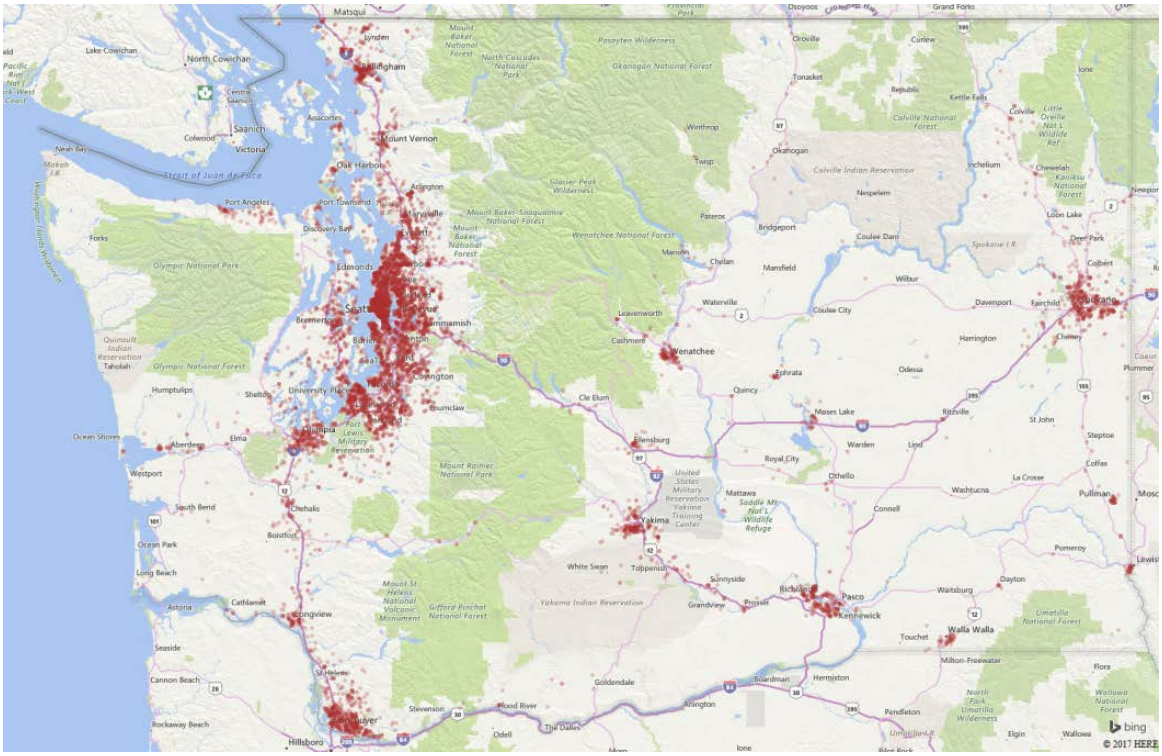
To date, the WSTR has enrolled 9,451 pairs, which includes 9,070 adult pairs (over 18), and 381 youth pairs (under 18). The following table presents a detailed breakdown of the overall demographics of our members.

Demographics of enrolled pairs (as of 6/30/2017)

Age	Percent
9 years old and under	3.3%
10-19 years old	1.0%
20-29 years old	16.8%
30-39 years old	27.0%
40-49 years old	14.7%
50-59 years old	13.2%
60-69 years old	14.0%
70 years old and over	10.1%
Ethnicity	
Hispanic/Latino	4.0%
Race	
White	89.9%
Black or African American	2.0%
American Indian or Alaska Native	0.6%
Asian	2.5%
Native Hawaiian or other Pacific Islander	0.4%
Some other race	1.4%
Two or more races	3.0%
Zygosity (self-report)	
Monozygotic (identical)	53.3%
Dizygotic (fraternal)	46.7%
Zygosity (DNA confirmed – pair N)	
Monozygotic	493
Dizygotic	231
Sex	
Male/Male pairs	28.1%
Female/Female pairs	50.1%
Male/Female pairs	21.8%

Where do our members reside?

We have members living in all 50 US states plus Washington DC, and around the world. The majority of our members (65%) live in Washington State, primarily in the Puget Sound region around Seattle. The following map shows the most concentrated areas in Washington:



Biological Specimens

In February 2017, we began the process of transferring our stored biological specimens located in freezers at the UW to our freezers at WSU Spokane.

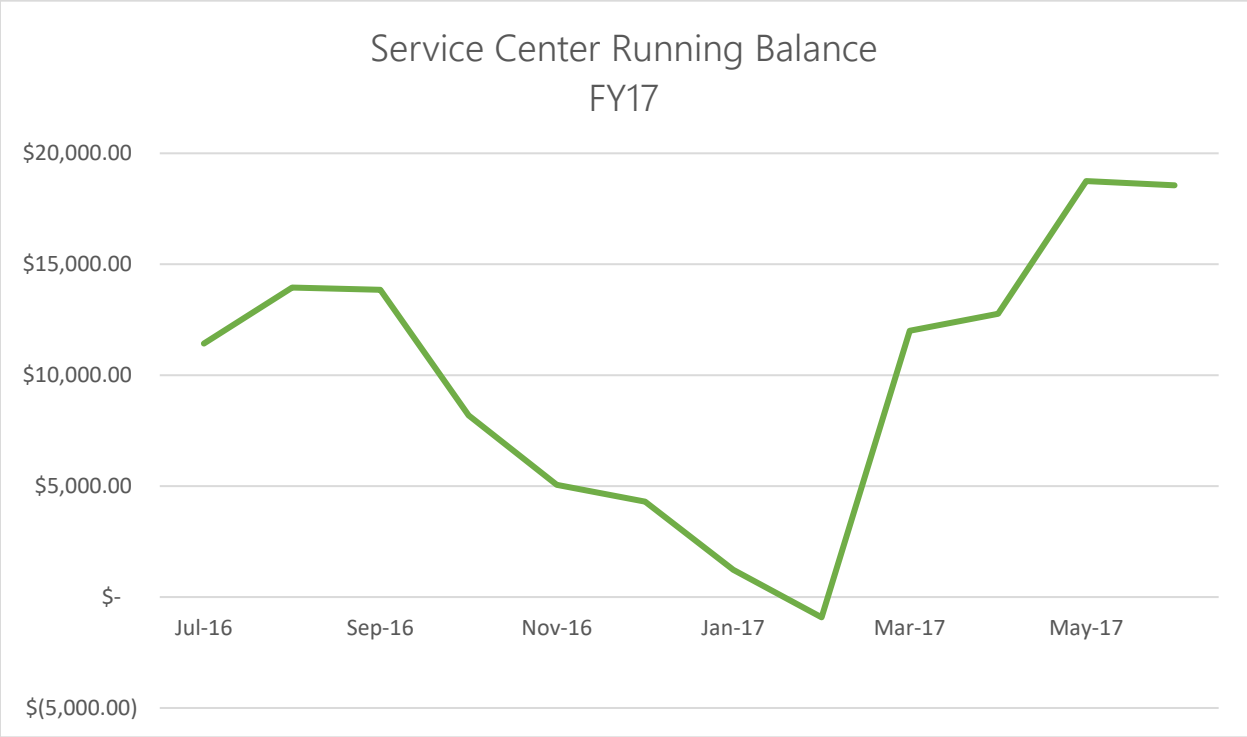
The following table summarizes the biological specimens that are currently available.

Sample type	Total Pairs*	Unique Pairs
Urine	501	437
Buccal cells	442	390
Plasma blue	318	300
Plasma green	315	297
Frozen whole blood	129	123
Processed DNA – whole blood	427	398
Processed DNA – Orgaene	4,049	3,874
Serum	545	467
Salivette (cortisol)	528	456

* Some twins may have participated in more than one study, allowing for potential longitudinal analysis of some samples.

Service Center

Use of the Twin Registry funds the service center, which supports recruitment and retention of twins in the Registry. The following graph shows the running balance during FY17:



The following table shows a breakdown of the expenses the service center incurred as well as sales during FY17:

01-Salary	(1,735.05)
07-Benefits	(603.14)
03-Consumable Goods and Services	(431.77)
03-WSU Overhead (8%)	(860.79)
Sales	**10,759.93**
Total Spending	(3,630.75)
Balance	7,129.18

The service center started FY17 with $11,424.50. The end-of-fiscal year overall balance was $18,553.68, demonstrating that the WSTR is in good financial health.

Current usage rates for the WSTR are summarized in Appendix A.

Active Research

Current grant-funded research projects

Epigenetic Determinants of Major Depression: A Monozygotic Discordant Twin Study

PI: Jinying Zhao, University of Florida and Eric Strachan, University of Washington
Project number: R01MH097018
Funding Agency: NIMH
Project dates: 8/15/2013-7/31/2018

Project Abstract

Major depressive disorder (MDD) is a devastating psychiatric disorder that affects millions of Americans. Despite substantial research, no specific risk factor has yet been identified as having a causal role in MDD. Epigenetic modifications, especially DNA methylation, are increasingly being recognized as a key mechanism involved in the pathogenesis of depression. However, the biological pathways linking aberrant methylation to depression remain poorly understood. This uncertainty greatly hampers our ability to implement early diagnosis, prevention and treatment for this debilitating disorder. The objective of this study is to identify functional epigenetic determinants for MDD. Our central hypothesis is that aberrant DNA methylation and resulting alterations in gene expression are associated with MDD. The rationale for the proposed research is that: once we know the epigenetic determinants for depression, we will be able to develop novel epigenetic markers and therapeutic targets for risk assessment, prevention and treatment of MDD and related psychiatric conditions. We proposed three specific aims: (1) Identify differentially methylated regions (DMRs) associated with MDD. This aim is to conduct an epigenome-wide DNA methylation analysis to identify epigenetic variations contributing to MDD in monocytes DNA from 100 monozygotic (MZ) discordant twin pairs from the University of Washington Twin Registry (UWTR), a large community-based twin registry in the U.S. (2) Replicate the top 50 ranked genes from Aim 1 in two independent samples, including 80 MZ discordant twin pairs recruited from the same registry and 36 postmortem brain tissue of well-characterized MDD patients and matched controls. (3) Determine the functional importance of the positive methylation findings in both blood and brain by profiling gene expression levels in each of the four brain regions (frontal cortex, hippocampus, amygdala, and cingulate cortex). Differential expressed genes related to MDD will be identified. Integrative analyses will be performed to elucidate the connections between DNA methylation patterns and gene expression of cognate genes in relation to MDD. The proposed study is the only one of its kind to identify functional epigenetic determinants for MDD in a well- matched MZ discordant twin sample, followed by replication in postmortem brain tissue, the affected organ in MDD. The work proposed here is expected to have an important positive impact, because genes with both differential methylation and expression are highly likely to provide novel epigenetic targets for prevention, intervention and treatment for depression and its related psychiatric conditions in addition to fundamentally advancing the fields of psychiatric genetics.

Progress to date

Potential twin pairs in this study are sent an invitation by email or mail, which has a link to complete a screening questionnaire to determine interest and basic eligibility. If twins are found eligible for further screening, the study PI at UW (Strachan) follows up with a phone call to conduct the Structured Clinical Interview for DSM Disorders (SCID). Twins who are eligible after completing the SCID are enrolled in the study. As of 6/30/17, this study has nearly completed recruitment of twin pairs, and will continue collecting data from a few additional pairs through the end of October 2017. Analysis of a batch of 45 pairs that received 450 IlluminaK processing has begun. Full processing of all pairs at Illumina 850K, and subsequent full analysis, will take place after enrollment and study visits are completed in the fall of 2017.

The following table summarizes recruitment and participation for this study:

	Contacted	Not interested	Not eligible	Completed study
MZ female pairs	549	83 (15%)	292 (53%)	67 (12%)
DZ female pairs	232	73 (31%)	52 (22%)	26 (11%)
MZ male pairs	305	67 (22%)	106 (35%)	27 (8%)
DZ male pairs	113	39 (35%)	29 (26%)	13 (12%)

Secondhand Smoke and Asthma: Mechanistic Outcomes of DNA Methylation in T Cells

PI: Kari Nadeau, Stanford University
Project Number: 5R01HL118612
Project Agency: NHLBI
Project Dates: 1/15/2014-12/31/2017

Project Abstract

Exposure to secondhand smoke (SHS) is associated with a greater lifetime risk of developing asthma, more severe asthma, and increased asthma hospitalizations for both children and adults. While much of the immunopathogenesis of asthma remains incompletely understood, key molecular events include changes in regulatory T cell (Treg) and effector T cell (Teff) activity in response to exposure to several air pollutants including SHS. Previous results from the Nadeau and Miller research groups suggest that Treg and Teff are epigenetically regulated, and their alterations affect the expression of several asthma genes and asthma-related clinical outcomes. While exposure to SHS has been shown to induce epigenetic alterations, and epigenetic changes in asthma genes may be associated with asthma, causal relationships have not been demonstrated. This proposal will try to establish a novel approach of SHS research by determining relationships between SHS exposure and asthma using uniquely linked mechanistic studies and an innovative study design. Key to this proposal is the intent to conduct studies in a well-phenotyped monozygotic twin (MZT) cohort including cases discordant on exposure to SHS and asthma that can determine the association of SHS-induced epigenetic marks, and the timing of this association, on asthma in the absence of differences in genetic backgrounds and in utero and early childhood environmental exposures, methodological limitations from prior studies. We hypothesize that exposure to SHS is associated with current asthma in adults, and this association is mediated through DNA methylation of asthma genes in Treg and Teff cells and the consequential downstream cellular events. Specifically, to understand the mechanisms of SHS-induced pathology in asthma and inflammation, we propose to: Aim 1: Test whether CpG methylation levels of specific genetic loci are altered in MZT discordant for smoking and asthma. Aim 2. Determine if minimization of exposure to SHS is associated with a decrease in methylation of Foxp3, IL-10, in Treg, and IFNy in Teff and an increase in methylation of IL-4 in Teff over time. Aim 3. Determine how methylation levels of Foxp3, IL-10, IFNy, IL-4 are influenced by never, prior (only in utero or only childhood), or current SHS exposure in asthmatic and nonasthmatic twins by estimating main effects and interactions and controlling for period of asthma onset. If the aims are achieved, this proposal should improve our understanding of the mechanisms by which exposure to SHS contributes to asthma and identify novel biomarker of smoke-related airway disease so that environmental policy and risk management can be developed more effectively, and screening and/or therapeutic interventions may be instituted earlier.

Progress to date

The WSTR referred twin pairs to the Stanford group in 2015. We sent a link to the screening form, in which the twins gave permission to be contacted by the Stanford coordinator. The table below summarizes recruitment and participation for this study:

	Contacted	Not interested	Not eligible	Scheduled
MZ female pairs	360	32 (9%)	20 (6%)	37 (10%)
MZ male pairs	188	62 (33%)	10 (5%)	15 (8%)

Data analysis is ongoing.

Validation and Application of Portable Particulate Device in the UW Twin Registry

PI: Edmund Seto, University of Washington and Glen Duncan, Washington State University

Project number: 5R21ES024715

Funding Agency: NIEHS

Project dates: 3/1/2015-2/28/2017 (NCE through 8/31/2017)

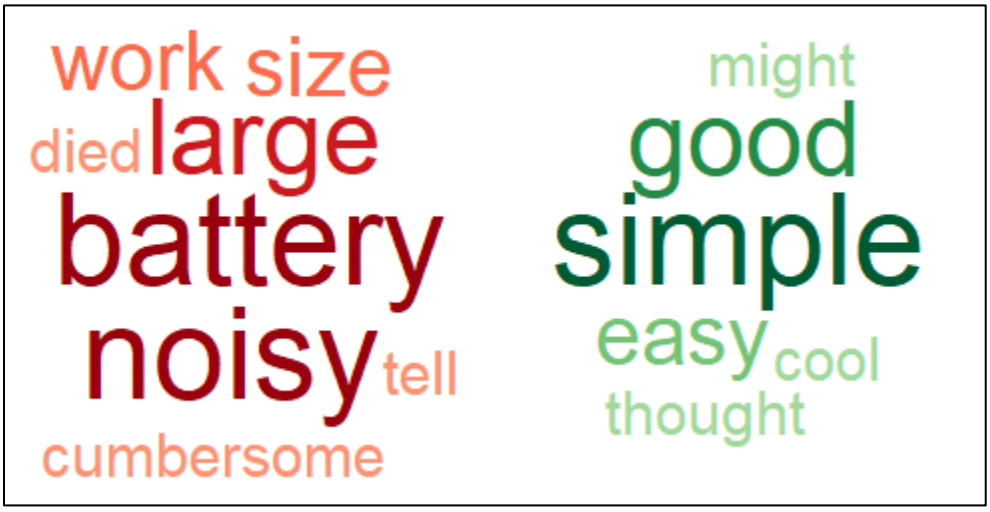
Summary of project

This research addresses the mission of the National Institutes of Environmental Health Sciences by increasing our understanding of how the environment influences human health through validation of a new wearable device that measures multiple environmental toxicants in real-time and space, called the Portable University of Washington Particle Monitor (PUWPM), and application in a genetically informed sample of adult twins from a community-based Twin Registry. The use of twins is unique in environment-based research because it will allow us to assess the associations between environmental exposures and health outcomes while controlling for genetic and shared environmental (familial) influences that might otherwise introduce selection biases into the choice of living environments that contribute to differential levels of exposures, and thus confound similar studies in unrelated individuals. Furthermore, our innovative methods will allow us to link environmental exposures with accelerometer and GPS-based measures of movement through space. Using GIS, we will capture spatially continuous variables relevant to the built environment at the same scale as the exposures and movement patterns. In the first phase the study (R21 phase), the design-feedback iterative cycle will be used to assess the feasibility and usability of the integrated PUWP monitor to assess multiple aspects of behavior and toxic exposures in 15 pairs of twins. Based on qualitative data obtained from focus groups and quantitative data from usability surveys, we will improve the design and ease of use of the PUWP through 2 or 3 iterative cycles. Concurrently, the validity of the PUWP will be established in these same 15 pairs compared to gold standard methods. In the second phase of the study (R33 phase), we will collect clinical measures including blood pressure, body mass index, waist circumference, and lung function (spirometry), as well as biologic measures including inflammatory cytokines and cortisol in a larger sample of 150 twin pairs. Using these measures, we will first compare associations between clinical/biological outcomes with PM 2.5 measures from the PUWP against their associations with exposure estimates based on ambient air quality models that are standard in the field. Next, we will determine the associations among air pollution, noise, and other environmental exposures from the integrated PUWP system, lifestyle behaviors including physical activity and diet, and psychosocial stress with the various clinical and biologic outcomes. Ultimately, our unique sample and methods will lead to new and important insights linking environmental, behavioral, and genetic aspects of chronic disease.

Progress to date

The WSTR recruited 5 pairs of twins to use the PUWP and provide feedback on its design. Two waves of testing are complete, with a third wave planned for mid-to-late July. After each wave of testing, we conduct a focus

group with the participants to gather feedback about what they liked and didn't like about using the device. The following word charts show the most frequently used negative (red) and positive (green) words in feedback after two waves of collection:



Improvements to battery life, size, and noise from the fan are anticipated with the next version of the PUWP. After completion of the R21 phase and final design considerations, the devices will be deployed in twin pairs recruited from the WSTR in the 3-year R33 phase of the project.

Neighborhood and genetic influences on alcohol misuse in a sample of twins

PI: Isaac Rhew

Funding source: University of Washington Royalty Research Fund

Project dates: 11/12/2015 – present

Summary of project

The goal of this research is to understand how neighborhood environments and genetic factors jointly influence risk for alcohol misuse. Greater insight into macro-environmental factors such as those occurring at the neighborhood-level could lead to ecologic prevention strategies with the potential for substantial population-level impact. While some evidence has emerged suggesting effects of neighborhood factors such as socioeconomic deprivation and alcohol outlet density on alcohol misuse, inference remains hindered because of challenges in accounting for "structural" confounding due to self-selection into neighborhoods. Further, as it has become recognized that genetic factors contribute significantly to alcohol misuse, it will be important to understand the particular environments where genetic susceptibility is greatest. Evidence for gene x environment interactions has increased, but little is known about how neighborhood-level environments modify genetic susceptibility to alcohol misuse. Such discoveries will advance our knowledge of the etiology of alcohol misuse and potentially guide neighborhood-level prevention strategies and identification of high-risk individuals. For this study, we capitalize on existing data from a community sample of approximately 4,000 adult twin pairs. The first aim of the study is to examine our hypothesis that alcohol misuse is associated with higher neighborhood deprivation and higher alcohol outlet density independent of individual-level socio-demographic characteristics. Using the co-twin design, we can address this question in an innovative way that allows us to control for genetic and shared environmental factors and thus reduce threats to validity from structural confounding. The unique characteristics of twin data will also allow us to conduct our second aim: to examine the relative contributions of additive genetic, shared environmental and unique environmental factors to alcohol misuse, and to examine whether genetic heritability will be stronger in neighborhoods with greater deprivation and higher alcohol outlet density.

Progress to date

The following publication was accepted during FY17 and is in press:

- Rhew IC, Kosterman R, Duncan GE, Mair C. Examination of cross-sectional associations of neighborhood deprivation and alcohol outlet density with hazardous drinking using a twin design. J Stud Alcohol.

A second paper is currently in development. An R01 application based on the findings of this project is anticipated for submission in February 2018.

Current non-grant-funded research projects

The following projects are supported by internal department funds.

Health and Wellbeing Survey Collection

PI: Glen Duncan

Project dates: 2010 – present

Summary of project

The Health & Wellbeing Questionnaire is an ongoing at-home study of the Twin Registry. The goals of this study are to understand how genetic and environmental factors influence human health, disease and behavior, and to see how the health of our members changes over time. This questionnaire was developed in 2009 when we were awarded a large ARRA infrastructure grant. One of the projects of this grant was to expand the size of our survey data repository. The Health & Wellbeing Questionnaire was developed from our previous surveys to collect data about health issues, habits, thoughts, and beliefs. Data collection began in 2010, when we mailed the first Health & Wellbeing Questionnaire to members of what was then the UW Twin Registry. In 2013 we developed an online version of the questionnaire, with invitations primarily sent by email. In 2015, with the move to WSU, we modified the questionnaire to be shorter and added new demographic, employment, and military questions. This questionnaire is currently sent to twin pairs every two years. If one twin completed it less than two years prior, we wait until both members of the pair have completed it more than two years prior, otherwise we have found that one twin will ask why they didn't receive an invitation to participate. When funding allows, or as requested, we work with the SESRC to send the questionnaire through the mail. Those completing the questionnaire on paper are significantly older (55.7 years) than those completing the questionnaire online (48.7 years).

Progress to date

The following table summarizes the number of Health and Wellbeing questionnaires that have been collected by twin pairs and twin individuals over time.

	Time 1	Time 2	Time 3
Twin pairs	4,332	1,603	691
Mean time between surveys	-	3.5	2.8
Twin individuals	10,650	3,639	1,474
Mean time between surveys	-	3.4	2.8

To date, we have published 17 peer-reviewed articles using data collected by this questionnaire.

Collaborative Project of Development of Anthropometrical Measures in Twins (CODATwins)

PI: Karri Silventoinen, University of Helsinki

Project dates: November 2013 – present

Summary of project

For over 100 years, the genetics of human anthropometric traits has attracted scientific interest. In particular, height and body mass index (BMI, calculated as kg/m^2) have been under intensive genetic research. However, it is still largely unknown whether and how heritability estimates vary between human populations. Opportunities to address this question have increased recently because of the establishment of many new twin cohorts and the increasing accumulation of data in established twin cohorts. We started a new research project to analyze systematically (1) the variation of heritability estimates of height, BMI and their trajectories over the

life course between birth cohorts, ethnicities and countries, and (2) to study the effects of birth-related factors, education and smoking on these anthropometric traits and whether these effects vary between twin cohorts. We identified 67 twin projects, including both monozygotic (MZ) and dizygotic (DZ) twins, using various sources. We asked for individual level data on height and weight including repeated measurements, birth related traits, background variables, education and smoking. By the end of 2014, 48 projects participated. Together, we have 893,458 height and weight measures (52% females) from 434,723 twin individuals, including 201,192 complete twin pairs (40% monozygotic, 40% same-sex dizygotic and 20% opposite-sex dizygotic) representing 22 countries. This project demonstrates that large-scale international twin studies are feasible and can promote the use of existing data for novel research purposes.

Progress to date

The WSTR contributed data to this project in 2013. Since that time, we have contributed to 6 published papers; 2 papers were recently accepted and are in press.

Heritability of Preferences

PI: Martin Reimann, University of Arizona

Project dates: 11/20/2015 – present

Summary of project

This study aims to examine heritable components of decision making (e.g., Simoson & Sela, 2010). In other words, we study the extent to which preferences are innate. Do preferences depend on nurture or nature (or both)? This research investigates how genes or the environment or a combination of the two impact preferences. Participants will respond to standard personality scales and will rate different visual and textual stimuli.

Progress to date

Data analysis is underway. The following table summarizes the recruitment and participation for this study.

	Contacted	Completed Survey	Not interested
MZ female pairs	804	185 (23%)	-
MZ female individuals	1,608	504 (31%)	62 (4%)
DZ female pairs	753	138 (18%)	-
DZ female individuals	1,506	460 (31%)	92 (6%)

The following publication was accepted during FY17 and made available online:

- Reimann M, Schilke O, Cook KS. Trust is heritable, whereas distrust is not. Proc Natl Acad Sci U S A.. doi: 10.1073/pnas.1617132114. Epub 2017 Jun 19.

Analysis of the visual stimuli responses is underway.

Correlates of Resilient Coping with Health Behaviors

PI: Dr. Vaughn Sinclair, Vanderbilt University

Project dates: 1/10/2017 – present

Summary of project

Mental health issues, obesity, smoking, substance abuse, and sedentary lifestyles are major problems in the U.S. population. There is a need to discover optimal coping behaviors that could enhance mental health and

promote health behaviors related to smoking, alcohol use, exercise, and weight management. There are many possibilities for examining genetic and environmental contributions to health behaviors and changes in health behaviors with this complex and rich database. We plan to examine a large array of research questions related to the shared heritability of resilient coping, personality traits such as neuroticism and conscientiousness, and various health behaviors. With these variables, we will examine these associations over time, along with the interactions of trauma history and depression. For example, one set of research questions will examine whether resilient coping levels at Time 1 predict changes in other variables (health behaviors; physical symptoms, and mental health) from Time 1 to Time 2. Interactions with personality variables at Time 1 could be added to these analyses. Another set of research questions will examine changes in resilient coping from Time 1 to Time 2, and assess whether these changes are similar in monozygotic (MZ) and dizygotic (DZ) twins. We will also examine whether changes in resilient coping from Time 1 to Time 2 reflect changes in mental health indicators (e.g., depression, anxiety, and perceived stress) and/or health behaviors. If these relationships are significant, there could be implications for interventions designed to enhance resilient coping that may affect mental health and health behaviors.

Progress to date

The dataset was created in January 2017, and data analysis is underway.

EpiGId: Epigenetic Gene Identifier - DNA methylation technology for forensic science

PI: Seth Faith and Deborah Silva, NC State University

Project dates: 2/8/2017 – present

Summary of project

Short tandem repeats (STRs) are considered as gold standards in human identification. However, the genomic information provided by these markers does not provide all answers necessary to overcome some challenging scenarios. One missing characteristic from STRs is the ability to differentiate between subjects that are monozygotic twins. Due to their shared DNA sequence, differentiation based on current identification markers is not possible and this causes problems as many criminal cases go unsolved, or when a paternity test is needed and the alleged father has a twin brother. One in 300 individuals has a twin and this poses some difficulty to a forensic investigation. Something noticeable, however, is the existence of discordant phenotypic traces between MZ twins, especially as they get older. Findings gathered from different studies show that epigenetic modifications of DNA and histones can play a primary role in phenotypic outcomes. The studies performed so far on epigenetics, most specifically on DNA methylation, concluded that different chromosome regions revealed distinct methylation patterns between MZ twins, and also that differences in DNA methylation levels were much more diverse in older monozygotic twins. So given these findings, our hypothesis is that DNA methylation markers can be explored and used to differentiate MZ twins. The purpose of our study is to identify differentially methylated sites in the human genome, using deep coverage methylation profiling microarray, to be used in the differentiation of monozygotic (MZ) twins, and develop a Next-Generation Sequencing epigenetic assay for twin differentiation and a bioinformatics tool able to process all data generated.

Progress to date

Finalizing approvals at NC State University.

Twin Study of Birth Weight and Reproductive Health

PI: Shayesteh Jahanfar, Central Michigan University

Project dates: 2/21/2017 – present

Summary of project

This study aims at investigating the role of two exposures (birth weight discordance and sex discordance) on health outcomes of twins. Birth weight discordance is defined as a disparity in birth weight between the larger and smaller infants of a twin set and it is identified as an important predictor of adverse fetal and neonatal health outcomes. A recent observational systematic review through a series of meta-analyses showed that exposure to growth discordance in twin gestation is significantly associated with perinatal mortality and morbidity. The relationship between birth weight discordance and adult diseases is not clear. Comparing the differences between twin pairs will isolate the pure effect of birth weight on the adulthood outcomes while holding innate abilities and family environments constant. Moreover, because twin have the same gestational age, the differences in birth weight between twins are attributable to differences in fetal growth rates. The unanswered question in the literature is that how differences in fetal growth rate relates to differences between twins during childhood, adolescent and adulthood. Correlation between birth weight per se and adulthood outcomes have been studied before, however, little is known about what would be the adverse health outcomes of each individual within a twin set. The differences between identical twins could be due to variation in fetal growth during intrauterine life or environmental factors after birth. For non-identical twins, such differences would be magnified, as they do not share identical genes. The question remains, if twins are born with severe birth weight discordance (more than 30%), how would their adult adverse health outcomes be different compared to twins born with smaller birth weight discordance (less than 30%)? Monozygotic twin pairs discordant for birth weight can provide a great model for studying the association between birth weight and health in adulthood while controlling for both genetics and postnatal rearing environment. Moreover, comparing adverse health outcomes after birth among twins with or without birth weight discordance provides a better understanding as to how important intrauterine environment is in determining adult health. Factors related to extra-uterine environment are categorized as shared and non-shared environment. Comparison between twins who are identical and lived apart compared to their counterparts who lived together may shed light on the impact of common environment on adverse health outcome.

Progress to date

IRB approvals finalized at WSU. Data collection set to begin in July 2017.

Student Projects

An Exploration and Cross Cultural Comparison of Mental and Physical Health Outcomes Associated with Single Parenthood

Student PI: Diana Dinescu, University of Virginia
Mentor: Eric Turkheimer, University of Virginia
Project dates: 2/1/2016 – present

Project Summary

Single parenthood is increasingly prevalent, and impacts communities in tangible ways. Economically, single parents have fewer resources and need to work more to maintain the same level of income as partnered parents. Socially, single parents benefit from less social support, maybe because do not have the time to contribute as much to a community as parents in a two-partner home. Emotionally, single parents may have greater needs, which may lead to alienation of their social support network and create a vicious cycle of lack of support and possible psychopathology. Despite the significance of this issue, relatively little is known about the nature of the mental or physical health outcomes of single parents, about the causal mechanisms behind these outcomes, and, consequently, about possible interventions. There are no investigations to date into this topic using genetically informed methods. Furthermore, the project has the unique advantage of being the first cross-cultural analysis of single parenthood using twin data. These characteristics make the present project a truly novel contribution to the field, and the beginning of a deeper investigation into the processes behind single parenthood. The proposed project will explore the association between single parenthood and health outcomes through a series of four studies. Study 1 is a descriptive analysis of single parenthood and health outcomes. Study 2 aims to eliminate nonrandom selection factors and greatly strengthen causal likelihood estimates of the association between single parenthood and depression. Study 3 aims to explore the association between single parenthood and other negative mental and physical health outcomes. Study 4 aims to conduct a cross-cultural comparison between Sweden and the US.

Progress to date

The following was published during FY17:

- Dinescu D, Turkheimer E, Beam CR, Horn EE, Duncan G, Emery RE. Is Marriage a Buzzkill? A Twin Study of Marital Status and Alcohol Consumption. Journal of family psychology : JFP : journal of the Division of Family Psychology of the American Psychological Association (Division 43). 2016;30(6):698-707.

Data analysis is still ongoing.

The relationship between walkability and low back pain: a co-twin control study

Student: Joshua Zadro, University of Sydney
Mentor: Paulo Ferreira, University of Sydney
Project dates: 1/5/2016 – 5/5/2016

Project Summary

Low back pain (LBP) is a global problem, resulting in disability and an enormous financial burden across many countries. Physical activity is effective for the management and prevention of LBP, with vigorous recreational physical activity demonstrating a strong protective effect. Despite this, people suffering from LBP reduce their physical activity, which will not only affect their LBP, but increase their risk of non-communicable disease. Therefore, physical activity promotion in people with LBP needs to be considered. Numerous methods are effective in increasing physical activity engagement; including changes to the built environment to improve

walkability e.g. continuity of sidewalks and proximity to recreation areas. Walkability is used to quantify the extent the built environment promotes walking for numerous purposes. However, the association between walkability and LBP has not been examined, and is important to consider before these strategies are implemented to promote physical activity in people with LBP. To get the clearest picture of the relationship between walkability and LBP we need to consider the role of genetics, since genetic factors have been shown to have a significant impact on LBP and physical activity engagement. In addition, genetics and shared environment play a role in influencing residential walkability, so need to be considered when investigating the relationship between walkability and LBP. Research investigating risk factors for LBP has recently utilized twins as a method of adjusting for the effects of genetics and shared environment. Twin pairs were usually exposed to a similar environment when growing up and share a proportion of their genetics, 50% in dizygotic (DZ) and 100% in monozygotic (MZ) twins. Therefore, twins allow us to adjust for the effects of genetics and shared environment, allowing us to understand the true association between walkability and LBP. Therefore, the primary aim of this study is to investigate the association between walkability and LBP, using a cross-sectional co-twin design to adjust for the effects of genetics and shared environment. Our secondary aim will be to investigate the correlation between walkability and self-reported physical activity. We expect to find a strong association between low walkability and LBP, and a strong positive correlation between walkability and self-reported physical activity.

Progress to date

The dataset was created in March 2016. The following was published during FY17:

- Zadro JR, Shirley D, Pinheiro MB, Bauman A, Duncan GE, Ferreira PH. Neighborhood walkability moderates the association between low back pain and physical activity: A co-twin control study. Prev Med. 2017 Jun;99:257-263.

A second dataset was created in May 2017, and data analysis is currently underway.

Genetically Informed Analysis of the SES-Health Gradient

Student: Erin Horn, University of Virginia
Mentor: Eric Turkheimer, University of Virginia
Project dates: 11/20/2015 – 5/31/2016

Project Summary

Socioeconomic status reliably predicts physical health, mental health, and health behaviors. This "health-SES gradient" is observed regardless of socioeconomic indicator, and holds true for both compositional (e.g., individual- and family-level SES indicators such as income or educational attainment) and contextual (e.g., neighborhood-level socioeconomic advantage, area-level income inequality) measures of socioeconomic status. Evidence from genetically informed studies suggests that this association is mediated by genetic pathways that are common to both SES and health, questioning the appropriateness of a causal interpretation for the SES-health gradient (as it relates to level of health). Further complicating the picture is a small body of genotype-by-environment interaction research suggesting that more socioeconomically deprived environments may potentiate genetic risk for expressing dysfunctional traits, although results from these studies are mixed regarding whether this represents a causal versus a selection process. More research is needed to understand how socioeconomic status affects level of health in the context of how it simultaneously affects the influence of genetic and environmental factors on health. The proposed dissertation research seeks to integrate these two perspectives in a broadscale, genetically informed approach to understanding the SES-health gradient.

Using contemporary samples of adolescent and adult American twin and sibling pairs raised in the same household (the National Longitudinal Study of Adolescent Health and the University of Washington Twin

Registry), the proposed dissertation will systematically evaluate the effect of SES—controlling for genetic confounds that often lead to biased or spurious findings—on mean levels of physical and mental health, including: chronic illnesses such as type 2 diabetes mellitus, asthma, and cardiovascular disease; immune functioning; health behaviors such as substance use or physical activity; and internalizing disorders such as anxiety and depression. We will also examine the influence of SES indicators on genetic risk for the same range of mental and physical health outcomes to understand whether SES makes some individuals more or less susceptible to expressing a particular health phenotype. Finally, the exacerbating or mitigating effects that SES has on the genetic or environmental pressures exerted by other factors on health (e.g., stress) will be examined to understand the SES-health gradient from a more holistic perspective. This dissertation will provide a clearer picture of what reducing individuals' socioeconomic burden will do—and won't do—for mental and physical health and well-being in 21st century America.

Progress to date

Data analysis is ongoing.

Grant-funded projects recently completed

A Twin Study of Obesity Pathogenesis using FMRI

PI: Ellen Schur
Project Number: R01DK089036
Funding Agency: NIDDK
Project Dates: 9/20/2011-8/31/2016

Project Abstract

Twin studies have provided decisive evidence for the hereditary nature of body weight regulation, demonstrating that individual differences in tendencies to gain weight can be explained by an interaction between genotype and nutrition. The exact mechanisms that connect genes to weight gain remain unknown, but they are crucial to understanding the pathogenesis of common obesity. Our goal is to identify central nervous system (CNS) mechanisms that contribute to genetic susceptibility to weight gain in the modern food environment. To this end, we will use neuroimaging to assess potential CNS mechanisms, and twin research methods to establish the mechanisms' genetic basis and their link to susceptibility to obesity. We, and others, have used functional magnetic resonance imaging (fMRI) to demonstrate that visual images of food powerfully stimulate brain areas active in regulating energy homeostasis, reward, and cognitive control of behavior. Whether these neural responses have a genetic basis is uncertain. Prior research suggests that obese persons have alterations in brain response to food cues that might promote overeating. Both human and animal studies also suggest that satiety is impaired in obese persons. To investigate these theories, we will use fMRI with visual food cues, augmented by functional connectivity analyses that examine brain function at a systems level. We will thereby provide new data on the extent to which observed differences in brain response to food cues among obese persons, as well as impaired satiety, represent genetic predispositions vs. potentially modifiable environmentally-mediated or acquired traits. We will implement our established fMRI protocol for measuring brain response to visual food cues in 2 twin samples recruited from the University of Washington Twin Registry. A random sample of 20 monozygotic pairs will allow us to test whether inherited factors can account for individual differences in brain response. We will also assemble a targeted sample of 21 monozygotic and 21 same-sex dizygotic twin pairs discordant for body mass index to: 1) determine whether body fat mass is associated with brain response to visual food cues and establish whether the association is mediated by inherited or acquired factors, and 2) determine whether impaired satiety is associated with body fat mass and, if so, whether impairments derive from peripheral or central abnormalities in satiety processing. All twins will be genotyped for variant alleles in the fat mass and obesity-associated (FTO) gene, one of the most common obesity susceptibility genes, in order to compare brain response to visual food cues in twins with and without FTO gene variants. This proposal has the potential to advance scientific knowledge of the brain's regulation of appetite and satiety. It will also provide insights into the CNS mechanisms by which inherited factors might predispose individuals to obesity, thereby guiding future research and targeting interventions for those at highest risk.

Progress to date

The following table summarizes recruitment and participation for this study.

	Contacted	Not interested	Not eligible	Completed study
MZ female pairs	273	39 (14%)	63 (23%)	26 (10%)
DZ female pairs	130	22 (17%)	39 (30%)	8 (6%)
MZ male pairs	136	18 (13%)	27 (20%)	18 (13%)
DZ male pairs	63	20 (32%)	10 (16%)	9 (14%)

To date, the following peer-reviewed articles have been published using data collected during this study:

- Bosch TA, Chow L, Dengel DR, Melhorn SJ, Webb M, Yancey D, Callahan H, De Leon MRB, Tyagi V, Schur EA. In adult twins, visceral fat accumulation depends more on exceeding sex-specific adiposity thresholds than on genetics. Metabolism. 2015 Sep;64(9):991-8.
- Melhorn SJ, Mehta S, Kratz M, Tyagi V, Webb MF, Noonan CJ, Buchwald DS, Goldberg J, Maravilla KR, Grabowski TJ, Schur EA. Brain regulation of appetite in twins. Am J Clin Nutr. 2016 Feb;103(2):314-22.
- Mestre ZL, Melhorn SJ, Askren MK, Tyagi V, Gatenby C, Young L, Mehta S, Webb MF, Grabowski TJ, Schur EA. Effects of Anxiety on Caloric Intake and Satiety-Related Brain Activation in Women and Men. Psychosom Med. 2016 May;78(4):454-64.

Data analysis is ongoing.

TWINStudy of Environment, Lifestyle Behaviors, and Health

PI: Glen Duncan
Project Number: R01AG042176
Funding Agency: NIA
Project Dates: 9/30/2011-5/31/2016

Project Abstract

The goal of this research is to determine how the built environment in which individuals live, work, and play in on a daily basis influences their lifestyle behaviors and health. We couple advanced methods in geospatial data management and analysis with cutting-edge technology, the multisensor board (MSB), to gather objective information about the built environment and lifestyle behaviors in real time and space. The MSB is a small wearable device with multiple sensing capabilities, including accelerometry, barometric pressure, and location, connected wirelessly to a WiFi enabled mobile telephone. Outdoor and indoor activities are monitored using GPS and WiFi signals to obtain data with high spatial resolution. The mobile phone has been adapted for use as an automated food intake program. We will use this integrated tool in a study of environmental influences on lifestyle behaviors and health in a community-based sample of adult monozygotic twins who were reared together but now live apart. With these tools and methods, we will create a unique and rich dataset linking rigorous measures of physical activity and eating in real time and space relative to locations in the built environment. This approach will build upon and extend our knowledge by measuring lifestyle behaviors in continuous time and space within and beyond the individual residential locations (neighborhoods) of twins. Using a co-twin control design, we will examine monozygotic pairs who live apart and determine how the home built environment influences levels of both walking and total physical activity, free of genetic and familial influences. Next, we will measure and compare location-based activity and eating episodes in real-time to investigate how often the twins use features of their home built environment that are associated with activity and eating. By measuring how many activity and eating episodes occur in the home built environment versus in distal built environments, including work, transit, and recreation-related settings, we will be able to determine whether proximity to features of the home built environment are associated with their use. Finally, we will measure associations among the built environment, lifestyle behaviors, and body mass index in twins who live apart by linking weight status with physical activity levels and food intake to determine if body mass index is associated with the built environment through these behaviors. Our scientific approach integrates conceptual models from the behavioral and social sciences with biological, computational, and physical measures in a genetically informative research design. This effort lays the critical groundwork to use an existing repository of phenotypic data and biological samples, including DNA, in future research to determine how specific genes interact with the environment to influence behaviors and health. Ultimately, our unique sample and scientific methods will lead to new and important insights linking environmental, behavioral, and genetic aspects of obesity and chronic disease.

Progress to date

A renewal R01 for this study will be submitted in July. The following table summarizes recruitment and participation:

	Contacted	Not interested	Not eligible	Completed study
MZ female pairs	355	40 (11%)	21 (6%)	103 (29%)
MZ male pairs	214	35 (16%)	9 (4%)	41 (19%)

To date, the following peer-reviewed articles have been published based on this study:

- Moudon AV, Drewnowski A, Duncan GE, Hurvitz PM, Saelens BE, Scharnhorst E. Characterizing the food environment: Pitfall and future directions. Public Health Nutr. 2013;16:1238-1243.
- Hurvitz PM, Moudon AV, Kang B, Saelens BE, Duncan GE. Emerging Technologies for Assessing Physical Activity Behaviors in Space and Time. Frontiers in Public Health. 2014;2:2.
- Duncan GE, Mills B, Strachan E, et al. Stepping towards causation in studies of neighborhood and environmental effects: How twin research can overcome problems of selection and reverse causation. Health & place. 2014;27:106-111.
- Cohen-Cline H, Turkheimer E, Duncan GE. Access to green space, physical activity, and mental health: a twin study. J Epidemiol Community Health. 2015;69:523-529.
- Cohen-Cline H, Lau R, Moudon AV, Turkheimer E, Duncan GE. Associations between fast-food consumption and body mass index: a cross-sectional study in adult twins. Twin Res Hum Genet. 2015;18:375-382.
- Duncan GE, Cash SW, Horn EE, Turkheimer E. Quasi-causal associations of physical activity and neighborhood walkability with body mass index: a twin study. Prev Med. 2015;70:90-95.
- Horn EE, Turkheimer E, Strachan E, Duncan GE. Behavioral and environmental modification of the genetic influence on body mass index: A twin study. Behav Genet. 2015;45:409-426.
- Hwang L-D, Hurvitz PM, Duncan GE. Cross Sectional Association between Spatially Measured Walking Bouts and Neighborhood Walkability. Timmermans H, ed. International Journal of Environmental Research and Public Health. 2016;13(4):412. doi:10.3390/ijerph13040412.
- Strachan E, Duncan G, Horn E, Turkheimer E. Neighborhood deprivation and depression in adult twins: genetics and gene×environment interaction. Psychol Med. 2017;47:627-638.

The Genetics & Epigenetics of Healthy Aging in Twins

PI: Sangkyu Kim, Tulane University
Project Number: P20GM103629
Sub-Project ID: 8393
Funding Agency: NIGMS
Project Dates: 8/1/2012-5/31/2017

Project Abstract

Aging can be defined as progressive deterioration of various biological functions with gradual increase in the risk of disease and death. This phenomenon is very complex with both genetic and non-genetic factors in action. The heritability of human longevity is estimated to be somewhere between 0.15 and 0.35. The action of genetic contributors can be modified by environment, resulting in altered risk of aging. One fundamental task in understanding its etiology is dissecting the relative contributions of genetic and non-genetic factors. My long-term research interest lies in the hereditary aspect of human aging and how the manifestation of the genetic basis is influenced by non-genetic factors during the life history of individuals. Based on twin study designs, I plan to identify genetic and epigenetic risk factors involved in human aging. In principle, the genetic

aspect of healthy aging in twins can be studied by investigating concordant dizygotic twins, and the epigenetic aspect by investigating discordant monozygotic twins with appropriate controls. The genetic study is to test the hypothesis that long-lived family members share common genetic variants that contribute to longevity and healthy aging. The epigenetic study is to test the hypothesis that the environmental contribution to the phenotypic variation of healthy aging is mediated by epigenetic mechanisms. To achieve these goals, I propose four Specific Aims. Aim 1 is to recruit twins who are at least 68 years old by means of the Mid-Atlantic Twin Registry (MATR), which is currently the largest twin registry in the U. S. According to data recently provided by the MATR, there are over 700 twin pairs available for this study. Aim 2 is to compile their healthy aging profiles and estimate their biological ages. For this purpose, we will survey participating twins for various health variables, which include medical history, physical and cognitive functioning. Aim 3 is to identify genes associated with healthy aging and longevity. For this aim, we will first identify genomic regions linked to healthy aging. Next, we will fine map the regions by applying case-control association analysis. Aim 4 is to establish DNA methylation as an epigenetic mechanism of healthy aging, and for this aim, we will study DNA methylation status of twins.

Progress to date

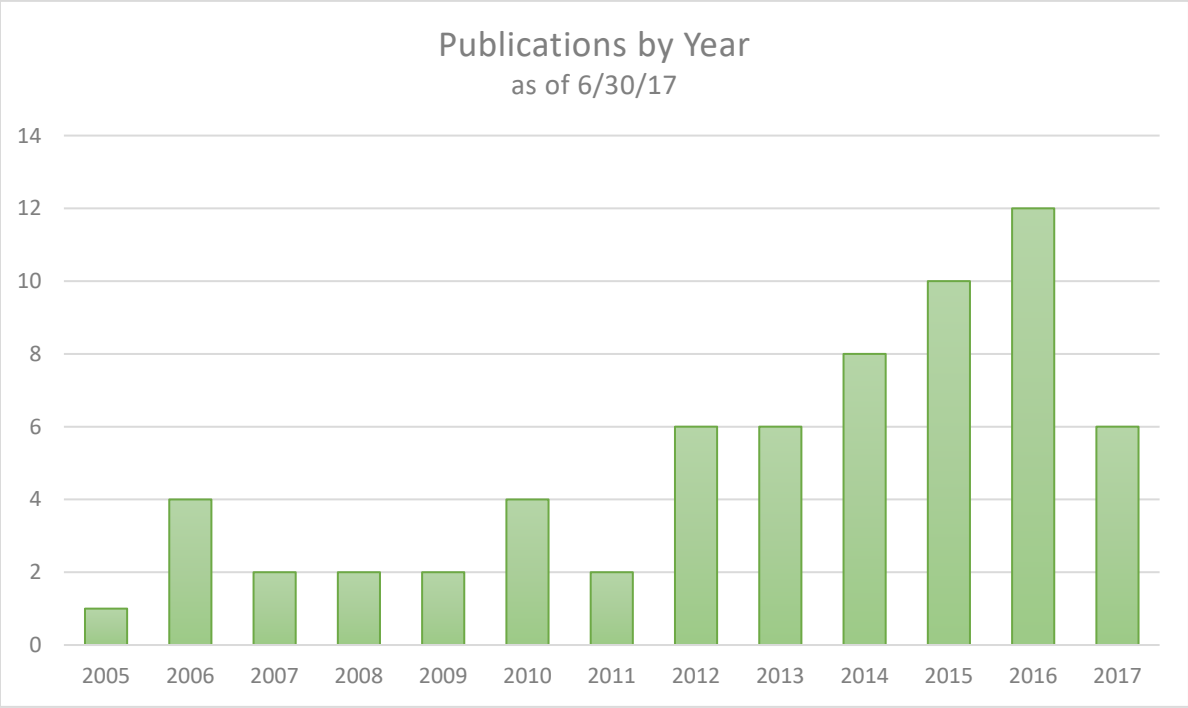
Data was collected from 2013-2015. The following table summarizes recruitment and participation:

	Contacted	Not interested	Not eligible	Completed study
MZ female pairs	34	0	12 (35%)	18 (53%)
DZ female pairs	136	10 (7%)	29 (21%)	78 (57%)
MZ male pairs	17	1 (6%)	5 (29%)	5 (29%)
DZ male pairs	79	7 (9%)	30 (38%)	33 (42%)

Data analysis is ongoing.

Publications

The following graph shows the number of publications per year since 2005, when the first peer-reviewed article using data from the Twin Registry was published. As of 6/30/17, we have published half the number of articles that were published in 2016, and we expect to meet or exceed the final 2016 publication count by the end of the calendar year.



Although this graph summarizes the number of publications by calendar year, the following lists are summarized by fiscal year.

FY16 (March 1, 2016 – June 30, 2016)

- Kleinhans NM, Yang CC, Strachan ED, Buchwald DS, Maravilla KR. Alterations in Connectivity on Functional Magnetic Resonance Imaging with Provocation of Lower Urinary Tract Symptoms: A MAPP Research Network Feasibility Study of Urological Chronic Pelvic Pain Syndromes. J Urol. 2016 Mar;195(3):639-45.

- Hwang LD, Hurvitz PM, Duncan GE. Cross Sectional Association between Spatially Measured Walking Bouts and Neighborhood Walkability. Int J Environ Res Public Health. 2016 Apr 8;13(4):412.

- Mestre ZL, Melhorn SJ, Askren MK, Tyagi V, Gatenby C, Young L, Mehta S, Webb MF, Grabowski TJ, Schur EA. Effects of Anxiety on Caloric Intake and Satiety-Related Brain Activation in Women and Men. Psychosom Med. 2016 May;78(4):454-64.

- Jelenkovic A, Sund R, Hur YM, Yokoyama Y, Hjelmborg JV, Möller S, Honda C, Magnusson PK, Pedersen NL, Ooki S, Aaltonen S, Stazi MA, Fagnani C, D'Ippolito C, Freitas DL, Maia JA, Ji F, Ning F, Pang Z, Rebato E, Busjahn A, Kandler C, Saudino KJ, Jang KL, Cozen W, Hwang AE, Mack TM, Gao W, Yu C, Li L, Corley RP, Huibregtse BM, Derom CA, Vlietinck RF, Loos RJ, Heikkilä K, Wardle J, Llewellyn CH, Fisher A, McAdams TA, Eley TC, Gregory AM, He M, Ding X, Bjerregaard-Andersen M, Beck-Nielsen H, Sodemann M, Tarnoki AD, Tarnoki DL, Knafo-Noam A, Mankuta D, Abramson L, Burt SA, Klump KL, Silberg JL, Eaves LJ, Maes HH, Krueger RF, McGue M, Pahlen S, Gatz M, Butler DA, Bartels M, van Beijsterveldt TC, Craig JM, Saffery R, Dubois L, Boivin M, Brendgen M, Dionne G, Vitaro F, Martin NG, Medland SE, Montgomery GW, Swan GE, Krasnow R, Tynelius P, Lichtenstein P, Haworth CM, Plomin R, Bayasgalan G, Narandalai D, Harden KP, Tucker-Drob EM, Spector T, Mangino M, Lachance G, Baker LA, Tuvblad C, Duncan GE, Buchwald D, Willemsen G, Skytthe A, Kyvik KO, Christensen K, Öncel SY, Aliev F, Rasmussen F, Goldberg JH, Sørensen TI, Boomsma DI, Kaprio J, Silventoinen K. Genetic and environmental influences on height from infancy to early adulthood: An individual-based pooled analysis of 45 twin cohorts. Sci Rep. 2016 Jun 23;6:28496.

FY17 (July 1, 2016 – June 30, 2017)

- Sinclair VG, Wallston KA, Strachan E. Resilient Coping Moderates the Effect of Trauma Exposure on Depression. Res Nurs Health. 2016 Aug;39(4):244-52.

- Silventoinen K, Jelenkovic A, Sund R, Hur YM, Yokoyama Y, Honda C, Hjelmborg Jv, Möller S, Ooki S, Aaltonen S, Ji F, Ning F, Pang Z, Rebato E, Busjahn A, Kandler C, Saudino KJ, Jang KL, Cozen W, Hwang AE, Mack TM, Gao W, Yu C, Li L, Corley RP, Huibregtse BM, Christensen K, Skytthe A, Kyvik KO, Derom CA, Vlietinck RF, Loos RJ, Heikkilä K, Wardle J, Llewellyn CH, Fisher A, McAdams TA, Eley TC, Gregory AM, He M, Ding X, Bjerregaard-Andersen M, Beck-Nielsen H, Sodemann M, Tarnoki AD, Tarnoki DL, Stazi MA, Fagnani C, D'Ippolito C, Knafo-Noam A, Mankuta D, Abramson L, Burt SA, Klump KL, Silberg JL, Eaves LJ, Maes HH, Krueger RF, McGue M, Pahlen S, Gatz M, Butler DA, Bartels M, van Beijsterveldt TC, Craig JM, Saffery R, Freitas DL, Maia JA, Dubois L, Boivin M, Brendgen M, Dionne G, Vitaro F, Martin NG, Medland SE, Montgomery GW, Chong Y, Swan GE, Krasnow R, Magnusson PK, Pedersen NL, Tynelius P, Lichtenstein P, Haworth CM, Plomin R, Bayasgalan G, Narandalai D, Harden KP, Tucker-Drob EM, Öncel SY, Aliev F, Spector T, Mangino M, Lachance G, Baker LA, Tuvblad C, Duncan GE, Buchwald D, Willemsen G, Rasmussen F, Goldberg JH, Sørensen TIa, Boomsma DI, Kaprio J. Genetic and environmental effects on body mass index from infancy to the onset of adulthood: an individual-based pooled analysis of 45 twin cohorts participating in the COllaborative project of Development of Anthropometrical measures in Twins (CODATwins) study. Am J Clin Nutr. 2016 Aug;104(2):371-9.

- Dinescu D, Turkheimer E, Beam CR, Horn EE, Duncan G, Emery RE. Is marriage a buzzkill? A twin study of marital status and alcohol consumption. J Fam Psychol. 2016 Sep;30(6):698-707.

- Jelenkovic A, Hur YM, Sund R, Yokoyama Y, Siribaddana SH, Hotopf M, Sumathipala A, Rijsdijk F, Tan Q, Zhang D, Pang Z, Aaltonen S, Heikkilä K, Öncel SY, Aliev F, Rebato E, Tarnoki AD, Tarnoki

DL, Christensen K, Skytthe A, Kyvik KO, Silberg JL, Eaves LJ, Maes HH, Cutler TL, Hopper JL, Ordoñana JR, Sánchez-Romera JF, Colodro-Conde L, Cozen W, Hwang AE, Mack TM, Sung J, Song YM, Yang S, Lee K, Franz CE, Kremen WS, Lyons MJ, Busjahn A, Nelson TL, Whitfield KE, Kandler C, Jang KL, Gatz M, Butler DA, Stazi MA, Fagnani C, D'Ippolito C, Duncan GE, Buchwald D, Derom CA, Vlietinck RF, Loos RJ, Martin NG, Medland SE, Montgomery GW, Jeong HU, Swan GE, Krasnow R, Magnusson PK, Pedersen NL, Dahl-Aslan AK, McAdams TA, Eley TC, Gregory AM, Tynelius P, Baker LA, Tuvblad C, Bayasgalan G, Narandalai D, Lichtenstein P, Spector TD, Mangino M, Lachance G, Bartels M, van Beijsterveldt TC, Willemsen G, Burt SA, Klump KL, Harris JR, Brandt I, Nilsen TS, Krueger RF, McGue M, Pahlen S, Corley RP, Hjelmborg JV, Goldberg JH, Iwatani Y, Watanabe M, Honda C, Inui F, Rasmussen F, Huibregtse BM, Boomsma DI, Sørensen TI, Kaprio J, Silventoinen K. Genetic and environmental influences on adult human height across birth cohorts from 1886 to 1994. Elife. 2016 Dec 14;5.

- Watson NF, Buchwald D, Delrow JJ, Altemeier WA, Vitiello MV, Pack AI, Bamshad M, Noonan C, Gharib SA. Transcriptional Signatures of Sleep Duration Discordance in Monozygotic Twins. Sleep. 2017 Jan 1;40(1).

- Strachan E, Duncan G, Horn E, Turkheimer E. Neighborhood deprivation and depression in adult twins: genetics and gene×environment interaction. Psychol Med. 2017 Mar;47(4):627-638.

- Beam CR, Dinescu D, Emery R, Turkheimer E. A Twin Study on Perceived Stress, Depressive Symptoms, and Marriage. J Health Soc Behav. 2017 Mar;58(1):37-53.

- Godfrey KM, Herbert M, Strachan E, Mostoufi S, Crofford LJ, Buchwald D, Poeschla B, Succop A, Afari N. Dexamethasone-suppressed Salivary Cortisol and Pain Sensitivity in Female Twins. Clin J Pain. 2017 Mar;33(3):246-253.

- Bogl LH, Jelenkovic A, Vuoksimaa E, Ahrenfeldt L, Pietiläinen KH, Stazi MA, Fagnani C, D'Ippolito C, Hur YM, Jeong HU, Silberg JL, Eaves LJ, Maes HH, Bayasgalan G, Narandalai D, Cutler TL, Kandler C, Jang KL, Christensen K, Skytthe A, Kyvik KO, Cozen W, Hwang AE, Mack TM, Derom CA, Vlietinck RF, Nelson TL, Whitfield KE, Corley RP, Huibregtse BM, McAdams TA, Eley TC, Gregory AM, Krueger RF, McGue M, Pahlen S, Willemsen G, Bartels M, van Beijsterveldt TCEM, Pang Z, Tan Q, Zhang D, Martin NG, Medland SE, Montgomery GW, Hjelmborg JVB, Rebato E, Swan GE, Krasnow R, Busjahn A, Lichtenstein P, Öncel SY, Aliev F, Baker LA, Tuvblad C, Siribaddana SH, Hotopf M, Sumathipala A, Rijsdijk F, Magnusson PKE, Pedersen NL, Aslan AKD, Ordoñana JR, Sánchez-Romera JF, Colodro-Conde L, Duncan GE, Buchwald D, Tarnoki AD, Tarnoki DL, Yokoyama Y, Hopper JL, Loos RJF, Boomsma DI, Sørensen TIA, Silventoinen K, Kaprio J. Does the sex of one's co-twin affect height and BMI in adulthood? A study of dizygotic adult twins from 31 cohorts. Biol Sex Differ. 2017 Apr 27;8:14.

- Zadro JR, Shirley D, Pinheiro MB, Bauman A, Duncan GE, Ferreira PH. Neighborhood walkability moderates the association between low back pain and physical activity: A co-twin control study. Prev Med. 2017 Jun;99:257-263.

News Articles

Occasionally findings from our publications are reported by newspapers and magazines. The following WSTR-related articles were "in the news" during FY17.

Pacific Standard: Marriage Drives us to Drink Less

New research confirms married people consume less alcohol than their single or divorced counterparts.

August 5, 2016 – Tom Jacobs
https://psmag.com/news/marriage-drives-us-to-drink-less#.362wtzxsr

WebMD: Skimp on Sleep and You Just May Wind Up Sick

Study of twins showed when someone is sleep-deprived, immune system weakens

February 9, 2017 – Alan Mozes
https://www.webmd.com/sleep-disorders/news/20170209/skimp-on-sleep-and-you-just-may-wind-up-sick#1

Phys.org: While trust is inherited, distrust is not: study

Research has shown that how trusting a person is may depend, at least in part, on his or her genes.

June 20, 2017
https://phys.org/news/2017-06-inherited-distrust.html

Contexts: Marriage and the genetic risk of depression

Christopher Beam, writing in the Journal of Health and Social Behavior, reports that being married significantly reduces genetic effects of perceived stress on depressive symptoms in the case of female twins.

June 24, 2017 – Justin Maietta
https://contexts.org/articles/marriage-and-depression/

Online Presence

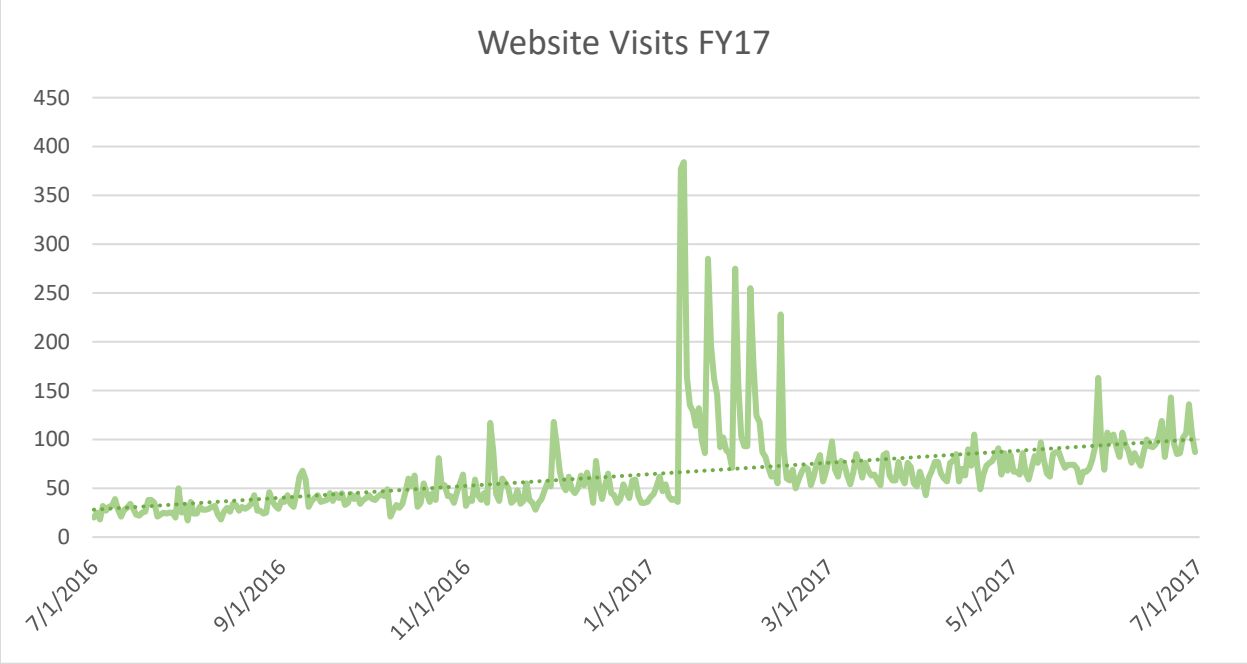
The Twin Registry began its online presence in 2012. Since that time, we have used our website and Facebook page to reach out to our members.

Our website is located at www.wstwinregistry.org

Our Facebook page is located at www.facebook.com/wstwinregistry

Website

Our website was launched in November 2015. The graph below shows the number of visits during FY17, which steadily increased over the year. We had over 23,000 visits to our website during FY17. New visitors spent less than 1 minute on our page and represented 89% of visits, while returning visitors spent nearly 2 minutes on our page.

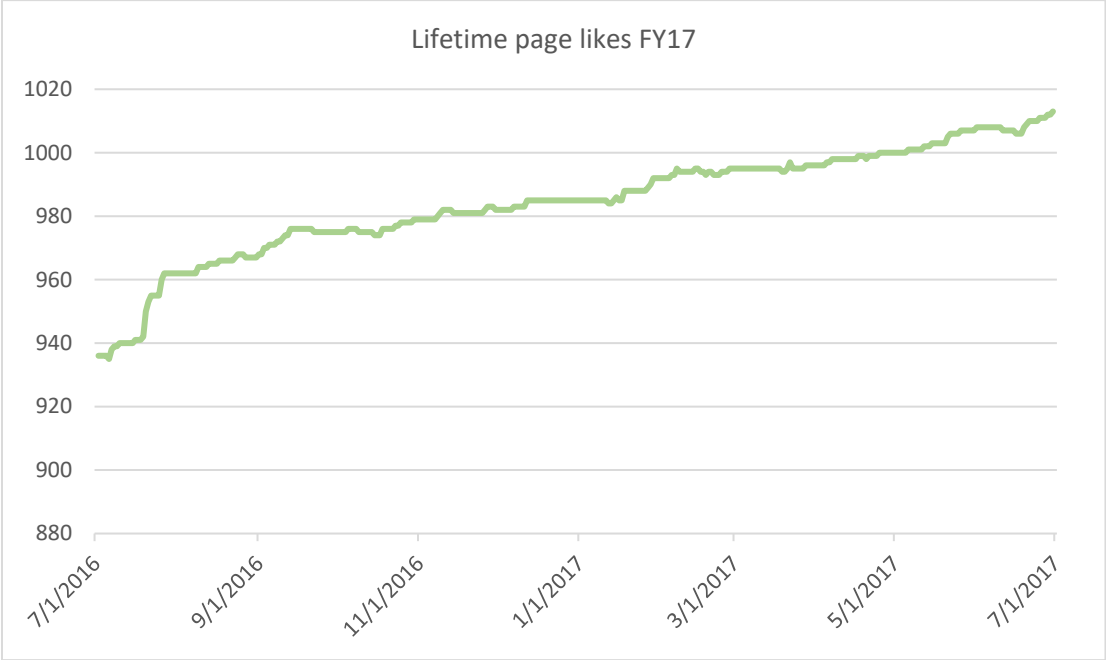


53% of visits to our website are from search engines, while 24% of visits are referrals from other websites. We use an online survey platform for collecting new survey data. At the completion of the survey, participants are redirected to our website, which thanks them for their participation and provides links to summaries about our research. Our largest mailing to date occurred in January 2017, which is where the spikes for website visits occur. After the survey platform referrals, the website for the DOL is our second largest referral source (http://www.dol.wa.gov/driverslicense/renew.html), followed by the NIH Genetics Home Reference website (https://ghr.nlm.nih.gov/primer/traits/twins).

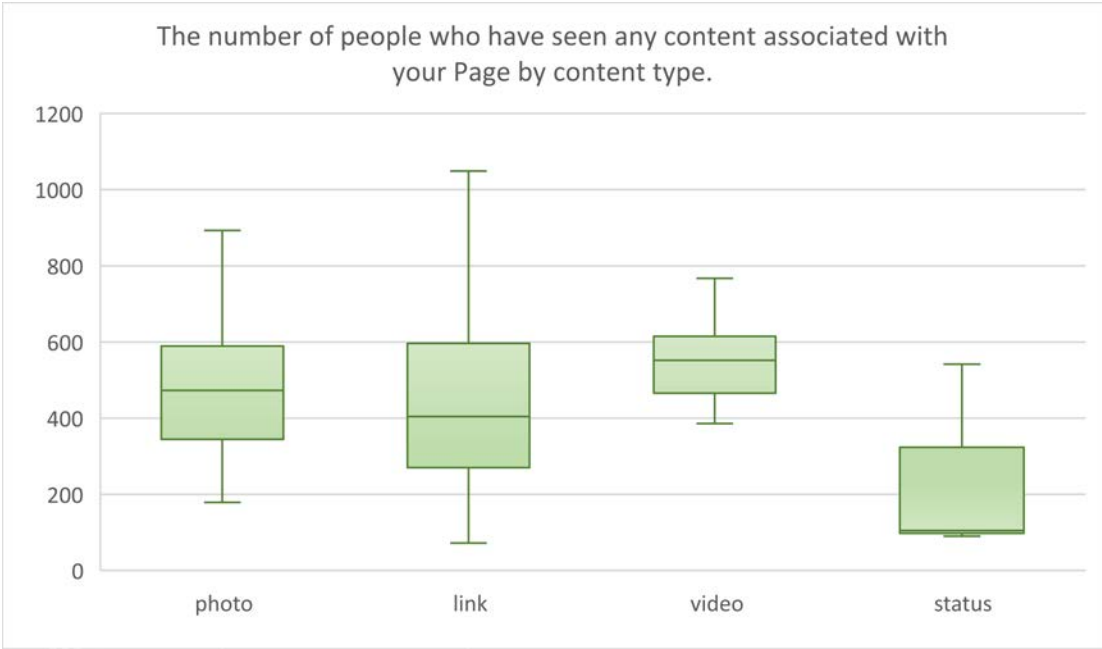
The demographics of visitors to our website largely reflect the demographics of the Registry. During FY17, 70% of visitors were female, and 32% were between the ages of 25 and 34.

Facebook

Our Facebook page has grown organically, primarily through links on our website and by sharing our posts. To date, we have 1,013 page likes, and that number continues to grow monthly. The following graph shows our page likes over the course of FY17.



We have found that posting every other day results in more content views compared to posting every day. The following graph shows the four types of content that we post, and how many views are associated with each type. Facebook's algorithm prioritizes video content in user news feeds, so that is something we will take in to consideration with content in FY 18.



Appendix A – Current service center rates

In addition to the significant infrastructure costs associated with recruitment and maintenance of the Washington State Twin Registry, requests for data by investigators and institutions can require considerable time and effort from Registry staff. For these reasons, the Registry charges fees to all investigators who wish to use Registry data or samples in their research. Without these fees, the resources necessary to enable investigators to work with Registry members would not be available. When research funding begins for an approved project, fees will be charged as services are provided (e.g., provision of data; screening and subsequent enrollment of twins by a Study Coordinator at the Registry). The schedule of access fees presented here is based on established Washington State University cost-accounting practices, and is subject to quarterly review. Investigators who are unable to issue a subcontract to the Washington State Twin Registry have the option of being billed by the Registry for all study-specific costs incurred. This option is intended solely to provide a more convenient method for non-Washington State University investigators to pay for study-specific costs. No revenue will be generated from this method and all study-specific costs will be billed to the investigator "at cost."

Rate #	Name	Short Description	Unit Base	WSU Rate	Non-WSU Academic Institution*
1	Survey Data	Cost for using data for specific twin pairs currently archived by the repository. This is also the rate for new analyses (i.e. new Specific Aims) on an existing sample.	Dataset	$999	$1,085
2	Geocoding	Cost for accessing and analyzing geocoding data for specific twin pairs currently archived by the repository.	Dataset	$4,299	$4,673
3	Stored samples	Cost for using specimens archived by the Washington State Twin Registry repository	Pair sample	$40	$43
4	Names & Addresses	Cost charged to investigators to send study invitations to twin pairs for an in-person twin study. This rate is charged after a study coordinator sends a batch of letters to a potential group of twins.	Mailing batch	$2,144	$2,331
6A	Research Study Assistant	Under general supervision, the Research Study Assistant performs varied support functions requiring knowledge and skills specific to the research study.	Hourly	$31	$33
6B	Research Study Coordinator	Under general supervision, the Research Study Coordinator coordinates the operations of research studies that involve human subjects and require knowledge and skills specific to the study.	Hourly	$34	$37
6C	Professional Research Coordinator	The Professional Research Coordinator develops research designs, strategies for recruitment and data management, and data collection methods; reports data; and manages budgets. This position may also supervise research staff.	Hourly	$46	$50
7A	Biostatistician	A study-specific Biostatistician collaborates with or offers consultation to the investigator.	Hourly	$66	$72
7B	Post-doctoral Behavioral Genetics Analyst	A study-specific post-doctoral-level Behavioral Genetics Analyst collaborates with or offers consultation to the investigator.	Hourly	$31	$33
7C	Faculty-level Behavioral Genetics Analyst	A study-specific faculty-level Behavioral Genetics Analyst collaborates with or offers consultation to the investigator.	Hourly	$150	$163
8	Faculty Co-Investigator	A study-specific faculty member collaborates with or offers consultation to the investigator regarding study design, objectives, monitoring progress, and supervision of study-specific support staff.	Hourly	$93	$101
9	Study-specific costs	To purchase study-specific supplies needed to implement research studies conducted by the Twin Registry	Itemized	Charged to investigator at cost	Charged to investigator at cost

* Includes 8% institutional overhead