

# University of Washington Twin Registry: Poised for the Next Generation of Twin Research

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The University of Washington Twin Registry is a unique community-based registry of twin pairs who join specifically to participate in scientific research. It was founded in 2002 to serve as a resource for investigators throughout the scientific community. Current enrollment exceeds 7,200 pairs, and plans are in place to increase enrollment to 10,000 pairs by 2015. In addition to serving as a recruitment base for new research studies, the registry maintains extensive and continually expanding survey data on physical and mental health, as well as a biorepository that includes DNA from more than 8,800 individual twins. The registry is engaged in linking member data to birth records and to diagnostic and procedure variables for hospital-based care provided to members in Washington State. It also incorporates several innovative variables relevant to the built and social environments, which were created by geocoding twin addresses and linking the resulting coordinates to geospatial information systems databases. This combination of existing data and biospecimens, characterizing a group of twins who are willing to participate in research, is a valuable resource for the new wave of twin studies. These include 'omics', epigenetics, gene-by-environment interactions, and other novel methods to understand human health.

■ **Keywords:** twin studies, twin registry, biospecimens, DNA, archival data

The community-based University of Washington (UW) Twin Registry began recruiting research participants in 2002 and has since grown to more than 7,200 twin pairs. The registry has collected an extensive body of survey and clinical data, including DNA samples from more than 8,800 individual twins. Twin volunteers have served as the recruitment base for dozens of federal and private research projects, whose findings have contributed to topics ranging from the molecular genetics of aging (Forsberg et al., 2012) to gene-by-environment interactions in sleep and obesity (Watson et al., 2012).

This unique resource grew out of the serendipitous discovery of a quirk in the Washington State Department of Licensing (DOL) application system. In Washington State, driver license identification numbers are based on a person's last name, first initial, and date of birth. Before the development of real-time computer networks, this formula occasionally led to the assignment of the same license num-

ber to both members of a twin pair. Therefore, alone among US states, the DOL in Washington State began asking every applicant if she or he was a member of a twin pair to avoid issuing duplicate numbers. Because Washington State also has legislation that allows data sharing across state agencies, the DOL's policy inadvertently laid the foundation for a valuable scientific resource.

This article presents current information on the size and scope of the UW Twin Registry, highlighting our recruitment procedures, our expanding collection of survey data

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and biospecimens, and continuing opportunities for new collaborations. Of particular importance, the registry now records data on birth weight and birth-related events, and will soon incorporate data on hospital-based diagnoses and treatments for twins who receive such care in Washington State. We also have an extensive database on built-environment and socio-demographic features of neighborhoods derived from precise geocoding (i.e., tagging with map coordinates) of twin addresses. Having more than tripled in size over the past decade (Afari et al., 2006), the UW Twin Registry is well positioned to work with collaborators worldwide on the next generation of twin research questions, ranging from proteomics, metabolomics, and other ‘omics’ to epigenetics, gene-by-environment interactions, and other novel approaches to uncovering the nature and dynamics of human health and disease.

### UW Twin Registry History

In 1998, investigators at UW began negotiating with the DOL and the Washington State Attorney General to obtain full access to the records necessary to construct a twin registry. By 2002, the UW Institutional Review Board and the office of the Attorney General approved the project, and the DOL began providing the names, contact information, and demographic characteristics of newly registered individual twins each week.

Recruitment efforts to populate the UW Twin Registry began in June 2002, when twins aged 18 years and older received an invitation packet to join the registry. The contents of the packet have evolved over the past decade, with the current iteration including an introductory letter, a registry brochure, an opt-out slip, a nominal incentive, and a brief enrollment survey. Non-responders receive a maximum of two follow-up packets, and are telephoned as needed to assess their interest and complete the enrollment survey. This instrument collects data on physical and psychological health, socio-demographics, and self-reported zygosity. Each twin who consents and completes the survey also provides his or her co-twin’s contact information. Co-twins are then contacted and recruited in a similar manner, since according to the registry’s ground rules, both members of each pair must participate in order for either one to become a member. Consent at the initial stage permits the registry to obtain new data from publicly available databases (although these acquisitions may require additional human subjects approvals), maintain the data repository indefinitely, and contact twins to invite them to voluntarily participate in research. Twins can also voluntarily provide unique personal identifiers that we can use for tracking and linking purposes.

### UW Twin Registry Expansion

In September 2009, the US National Institutes of Health (NIH) awarded substantial funding to the UW Twin Reg-

istry and its affiliated investigators through the mechanism of a Grand Opportunity grant, as instituted by the American Reinvestment and Recovery Act. This funding enabled investigators to expand the registry and its data collection as a state-of-the-art research infrastructure and contribute to the accelerating pace of genomic and environmental research. At the time of the award, 2,631 twin pairs were enrolled in the registry, 280 twin pairs had contributed to the DNA repository, and the registry infrastructure was sustained by a cost-center model that charged researchers for their use of registry data. The goals of the Grand Opportunity grant were to expand enrollment, collect new survey data and DNA specimens, and generate new data from birth records, hospital records, and geocoding. We discuss each goal in turn.

### Expanding Enrollment

#### Membership Invitations

Since its inception, the UW Twin Registry has been receiving the names, contact information, and demographic characteristics of approximately 60 new individual twins each week from the DOL. Before 2009, the DOL included the question on twin status only on new driver license applications. At our request, the application process was modified to add that question to all renewal applications, whether online, in-person, or mail-in. Launched in September 2010, this additional data collection effort was seamlessly integrated into our existing data transfer protocol. The number of individual twins whose data are received from the DOL averages 300 per week.

New names and contact information are entered into a contact database — which is separate from the actual registry — and compared to previous records to prevent duplicate contacts. Once the contact list is cleaned, we engage in the recruitment procedures described above. Because the participation of both members of a twin pair is required, research assistants telephone co-twins to encourage the return of surveys. Since the inception of the registry, more than 57,000 individual twins have received invitation packets, and current enrollment is more than 7,200 pairs. We expect the registry to surpass 10,000 pairs by 2015.

#### Mailing and Follow-Up Strategy

We have conducted several experiments to identify factors that might influence response rates for our invitation packets. Specifically, we have tested the success of mailing our initial enrollment packet in the following combinations: FedEx plus \$5 incentive, United States Postal Service (USPS) Priority Mail plus \$5 incentive, USPS Priority Mail plus \$2 incentive, and oversized first class envelope plus \$2 incentive. Analysis of these data is still in process, but initial results suggest that the various incentive amounts have a modest impact on response rates. For example, the largest proportion of mailings (66%) goes out to twins who renew

a license or ID card online. In this group, changing the incentive from \$5 to \$2 resulted in a 15% decrease in response rates.

Given the cost of including \$5 incentives in all ongoing initial recruitment mailings, balanced with the higher response rate for the \$5 incentive and the need to moderate expenses, we are planning another experiment to determine the impact of providing compensation only after completion of the initial enrollment survey. This strategy will use gift cards as compensation, enabling new enrollees to spend their gift cards by choosing from a large list of popular retailers, by cashing out, or by donating to charity. The value of these gift cards never decreases, and the registry incurs no out-of-pocket cost except the dollar amount of the gift cards. On top of the significant savings provided by this switch to post-enrollment compensation, the new process can substantially reduce the administrative burden caused by our previous compensation system.

In addition to a vast amount of response rate data, we have also been able to revisit our assumptions on ideal times for making follow-up telephone calls to twins. Past experience indicated that ideal calling times fell between the hours of 5:00 p.m. and 8:00 p.m. on weekdays. In a recent re-analysis of call data, we assessed current trends in call time success, noting significant changes. Preliminary analyses now suggest that optimum calling times have shifted to 12–2:00 p.m. and 4–5:00 p.m. on weekdays. While many explanations are possible, we speculate that increased use of mobile phones is the primary factor. Potential participants may be more likely to answer a mobile phone call during relatively slow periods of the workday than during non-working hours.

### Updated Recruitment Materials

As part of our recent expansion, we have overhauled all recruitment materials. Revisions were based on feedback from prospective members as well as on our implementation of new protocols to improve quality control throughout the recruitment process, including an easier opt-out mechanism. In addition, we launched the registry's first online recruitment survey, which enables eligible twins to enroll without completing a paper survey. We anticipate that the online enrollment mechanism will increase response rates and drastically reduce the administrative burden on Registry staff.

### Member Retention

To enhance retention, we also improved the visual appeal of all our contact materials. These efforts included rebranding of the UW Twin Registry with a look that strengthened our association with UW and with twin research. In 2011, we sent a new packet to all registry members to celebrate our rebranding and demonstrate our appreciation of their participation. The packet included a key chain, window decal, newsletter, and thank-you letter. Registry members also re-

ceive yearly birthday cards and frequent newsletters, which furnish our primary means of updating contact information. We have also employed the use of the private search service LexisNexis to locate members lost to follow-up.

### Member Characteristics

The UW Twin Registry includes a community-based cohort of relatively young, well-characterized twins who are willing to participate in research studies and are representative of the general twin population in Washington State (Afari et al., 2006). Mean age at time of enrollment is 37 years (range = 18–94); 86% are White; 93% have a high school education or higher; and 47% are married or cohabiting. As Table 1 indicates, female pairs make up 49% of the registry, and 53% of pairs are monozygotic (MZ; identical) according to self-report data. Table 2 shows a partial list of registry phenotypes by zygosity and frequency. Since the question on twin status was added to the DOL renewal system, the average age of participants has steadily increased (from 32 in 2006 to 37 in 2012), providing more opportunities for research with older twins. In addition, we recently completed a pilot study for which we contacted parents of registry members, finding that a substantial fraction of parents were also willing to participate in research.

### Building the Repository

One of the most important features of the UW Twin Registry is its repository of survey data and biospecimens (Tables 3–5). The repository includes data from numerous successive surveys on demographics and physical and mental health, along with biospecimens that include whole blood, urine, and saliva samples for use in DNA and other analyses. Ongoing studies of diverse conditions, such as depression, diabetes, obesity, chronic widespread pain, and immune function, have already benefited from this resource.

### DNA Repository

Our DNA repository now holds information on more than 4,250 twin pairs. To build this repository, all UW Twin Registry members were invited to participate in a DNA collection campaign. We used Oragene DNA Self-Collection saliva kits (DNA Genotek Inc., Kanata, Ontario, Canada) and offered compensation ranging from \$20 to \$50. These kits offer a safe, non-invasive approach to collecting DNA, with an error rate of only 3% (i.e., 3% of samples have insufficient saliva for analysis). Additionally, because saliva is considered a non-infectious substance, it was possible to ship samples under the more relaxed classification of 'Exempt Human Specimen', further lowering the burden on participants and allowing us to complete data collection entirely through the USPS.

The saliva collection effort was launched in 2010, when members began receiving an introductory letter followed by a saliva kit with return materials. Extensive new protocols

**TABLE 1**  
Demographic Characteristics of the University of Washington Twin Registry Twins<sup>a</sup>

	All (N = 14,048)	MZ/MM (N = 2,650)	DZ/MM (N = 1,224)	MZ/FF (N = 4,630)	DZ/FF (N = 2,062)	DZ/MF (N = 3,150)
Age at survey, mean years (SD)	37.2 (17.7)	36.2 (17.6)	38.5 (18.7)	35.9 (16.6)	39.7 (18.0)	38.2 (18.5)
Marital status, %						
Single	42	48	47	39	34	43
Married	41	40	40	41	44	39
Widowed	2	1	1	2	3	2
Divorced	7	5	6	8	10	8
Separated	1	1	2	1	1	1
Living with partner	7	5	6	8	7	7
Not reported	<1	<1	<1	<1	1	1
Hispanic, %	4	3	4	5	3	3
Race, %						
American Indian or Alaska Native	1	1	<1	1	1	1
Black or African American	2	2	2	2	2	2
Native Hawaiian or Pacific Islander	<1	<1	<1	<1	<1	<1
Asian	3	4	1	3	2	1
White	86	85	90	84	89	88
Other	2	2	2	3	2	2
More than one race	3	3	3	4	2	2
Not reported	2	2	2	3	2	2
Completed education, %						
<9th grade	<1	1	1	0	0	1
9th–11th grade	7	8	8	5	5	7
12th grade or GED	25	26	27	23	25	26
Some college, vocational school	34	31	30	37	35	35
Bachelor's degree or higher	33	33	33	34	35	31
Not reported	1	1	1	<1	<1	1

Note: <sup>a</sup>n = 332 twins missing from zygosity/sex columns due to indeterminate zygosity.

MZ = monozygotic; DZ = dizygotic; MM = male–male; FF = female–female; MF = male–female; SD = standard deviation; GED = graduate equivalency diploma.

**TABLE 2**  
Self-Reported Health Conditions by Zygosity<sup>a</sup>

	Monozygotic twins (n = 7,280)	Dizygotic twins	
		Same sex (n = 3,286)	Opposite sex (n = 3,150)
Cardiovascular conditions			
High blood pressure	1,206 (16.6%)	630 (19.2%)	633 (20.1%)
Heart attack or disease	184 (2.5%)	118 (3.6%)	98 (3.1%)
Blood clots in legs or lungs	105 (1.4%)	55 (1.7%)	59 (1.9%)
Chronic pain and fatigue			
Low back pain	2,101 (28.9%)	1,000 (30.4%)	990 (31.4%)
Herniated or slipped disc	518 (7.1%)	236 (7.2%)	246 (7.8%)
Migraine headaches	1,199 (16.5%)	517 (15.7%)	487 (15.5%)
Chronic tension headaches	528 (7.3%)	244 (7.4%)	233 (7.4%)
Chronic fatigue syndrome	135 (1.9%)	79 (2.4%)	58 (1.8%)
Fibromyalgia	116 (1.6%)	83 (2.5%)	50 (1.6%)
Temporomandibular joint disorder	327 (4.5%)	153 (4.7%)	123 (3.9%)
Irritable bowel syndrome	499 (6.9%)	221 (6.7%)	204 (6.5%)
Neuropsychiatric conditions			
Depression	1,511 (20.8%)	748 (22.8%)	656 (20.8%)
Panic/anxiety attacks	961 (13.2%)	451 (13.7%)	422 (13.4%)
Attention deficit hyperactivity disorder	297 (4.1%)	181 (5.5%)	199 (6.3%)
Posttraumatic stress disorder	292 (4.0%)	138 (4.2%)	110 (3.5%)
Seizures or epilepsy	182 (2.5%)	79 (2.4%)	79 (2.5%)
Chronic diseases			
Diabetes	271 (3.7%)	177 (5.4%)	160 (5.1%)
Asthma	1,085 (14.9%)	480 (14.6%)	452 (14.3%)
Gastroesophageal reflux	681 (9.4%)	302 (9.2%)	299 (9.5%)
Sinus and allergies			
Chronic sinus problems	660 (9.1%)	282 (8.6%)	281 (8.9%)
Allergies	2,457 (33.8%)	1,091 (33.2%)	1,030 (32.7%)
Speech and hearing			
Hearing loss	717 (9.8%)	363 (11.0%)	402 (12.8%)
Speech problems	433 (5.9%)	199 (6.1%)	179 (5.7%)
Kidney stones	334 (4.6%)	161 (4.9%)	175 (5.6%)
Breast cancer	75 (1.0%)	44 (1.3%)	44 (1.4%)

Note: <sup>a</sup>This is a partial list of UW Twin Registry phenotypes.

**TABLE 3**  
Questionnaire Assessment Domains

Assessment domain	2002–2007 Recruitment Survey (n = 5,717)	2008–present Recruitment Survey (n = 8,693)	2004–present Module Survey (n = 650)	2006 & 2008 Health Survey (n = 3,072)	2010–present Health & Wellbeing Survey (n = 8,736)
Sociodemographics	X	X	X	X	X
Zygosity	X	X			
Height and weight	X	X	X	X	X
Medical history	X	X	X	X	X
Physical activity	X	X	X	X	X
Sleep	X	X	X	X	X
Eating habits		X		X	X
Allergies		X	X	X	X
Health functioning	X	X	X	X	X
Alcohol use	X	X	X	X	X
Tobacco use	X	X	X	X	X
Pain conditions	X	X	X	X	X
Fatigue	X	X	X	X	X
Head injury		X		X	X
Depression	X	X	X	X	X
Anxiety	X	X	X	X	X
Posttraumatic stress	X	X		X	X
Resilient coping		X			X
Distress			X		
Perceived stress			X	X	X
Cognitive functioning			X		X
Home and work toxic exposures			X		
Occupational exposures			X		
Food frequency			X		
Five-factor personality					X

and data management systems were implemented to support project recruitment efforts. Out of 11,893 individuals invited to participate, we received kits from 8,868 (75% response rate), representing 3,991 completed twin pairs and 886 singletons whose co-twins did not respond. These kits were immediately processed for DNA by the registry's central lab and are now available for use by researchers.

### Survey Data Repository

The second component of the repository expansion effort was a data collection campaign using a comprehensive, 12-page phenotyping survey. As with saliva collection, all registry members were offered the option of participating, with compensation ranging from \$30 to \$50. Response rates were similar to those for the saliva kits, with 8,736 out of 11,774 individuals (74% response rate) returning the surveys, representing 3,735 completed pairs and 1,266 singletons. These surveys were distributed 1 month after the saliva kit, regardless of individual response to the kit. Telephone follow-up was conducted as staff time allowed, and participants received payment for each component after it was received. We also had good results from our efforts to collect both saliva and surveys from registry members residing outside the United States, supporting the feasibility of international sample collection. After 3 years, we had collected completed surveys and DNA from both members of 3,561 pairs.

**TABLE 4**  
In-Person Measurements

Assessment domain	2004–present Module (n = 1,042)
Vital signs	X
Hip and waist circumference	X
Spirometry	X
Pulse oximetry	X
Six-minute walk	X
Dolorimetry	X

### In-Person Phenotyping

Since its inception, the UW Twin Registry has been collecting supplementary data and biospecimens from twins who present for in-person study visits conducted by investigators recruiting participants from the registry. Known as the 'Module', this collection of supplementary data and specimens was intended to support pilot studies for phenotypes of general interest (e.g., self-reported health, depression, physical activity, and sleep) and the data and specimens are described in Tables 3–5. To obtain additional phenotyping data on members' experience of pain, we used successful recruitment strategies developed for previous studies to recruit and examine an in-person sample of 200 healthy twin pairs. This sample was balanced for sex (94 male–male and 106 female–female pairs) and zygosity (107 MZ and 93 same-sex dizygotic pairs). In addition to the

**TABLE 5**  
**Biorepository Specimens**

Biological sample	2004–present Module ( <i>n</i> = 1,042)	2010 Oragene ( <i>n</i> = 8,868)
Sera	X	
Plasma	X	
Urine	X	
Buccal swab	X	
Saliva swab	X	
Whole blood	X	
DNA		X

standard elements of the Module, twins underwent a multi-modal evaluation of pain sensitivity, including cold, heat, and pressure stimuli; completed a battery of standardized self-report measures; received a physical examination; and provided biospecimens. The latter included whole blood drawn for serum, plasma, and DNA/RNA extraction. We also collected urine samples, as well as saliva obtained by using Oragene DNA Self-Collection saliva kits, saliva plugs, and buccal swabs. C-reactive protein and cytokines that are known to influence the production and up-regulation of C-reactive protein (IL-1, IL-1 $\beta$ , TFG-1 $\beta$ , IL6, TNF- $\alpha$ ) were assayed from blood plasma at the UW Immunology Division laboratory, using standard laboratory procedures. Purified genomic DNA was extracted from whole blood and used for genotyping a small set of genes previously documented to be related to pain sensitivity or clinical pain syndromes. Genotyping of rs6746030 in SCN9A and rs734784 in KCNS1 is now complete, and preparations for other single-nucleotide polymorphism analyses are underway. While our own planned analyses focus on understanding the phenotypic and genotypic mechanisms underlying pain sensitivity and its association with C-reactive protein, the breadth and depth of these data, especially in combination with other data available in our collection, provide a unique opportunity for investigators to address diverse research questions. Of particular importance, these data can be used to conduct bivariate biometrical genetic analyses to assess the effects of specific gene polymorphisms on the link between pain and other characteristics.

### Assigning Zygosity

Assignment of zygosity is critical to understanding the contributions of genes and environment to phenotypes. All same-sex registry members are assigned zygosity based on self-reported information about childhood similarity. This strategy is common in most twin registries worldwide and can be used to classify zygosity with an accuracy of 95–98% compared with biological indicators (Eisen et al., 1989; Torgersen, 1979). The algorithm that we use to predict zygosity from self-report data is periodically updated whenever new DNA-based zygosity assignments are added to the registry from ongoing studies.

## New Data Domains

In addition to enlarging our collection of existing types of survey and biospecimen data, UW Twin Registry investigators have begun to make new domains of data available for research. The first new domain comprises data on birth and birth events, and the second domain comprises hospital-based diagnoses and treatment. The third comprises data on the neighborhoods where registry members live, including characteristics of the built environment as well as socio-demographic factors.

### Birth Records

The Washington State Department of Health maintains databases of vital statistics, records of hospitalizations, and other public health variables. The UW Twin Registry recently began linking vital statistics data to twin records to explore the hypothesis that adult health and disease have fetal origins (e.g., Barker, 2007). For registry members born in Washington State between 1954 and 1979, we have limited data on birthplace and parental age and race. For members born between 1980 and 1994, however, we have much more extensive data, including twin variables such as fetal distress, gestational age, delivery method, birth weight, and Apgar score (an assessment of newborn health), as well as parental variables such as smoking and other health behaviors. Using these data, we plan to investigate whether adverse conditions in utero or at birth are associated with impaired physical or mental health in adulthood. Given our extensive registry data, investigators can now examine the link between birth variables and such outcomes as cancer, asthma, chronic pain, depression and anxiety disorders, sleep disorders, chronic stress, eating dysregulation, obesity, and immune system functioning (especially inflammation).

### Hospital Records

The Registry maintains extensive self-reported medical histories from member twins, including histories of hypertension, heart disease, stroke, diabetes, kidney disease, multiple sclerosis, epilepsy, breast and other cancers, and depression. We are now able to link these rich data to the Washington State Department of Health's Comprehensive Hospital Abstract Reporting System, a database that stores hospital discharge information from 1987 to the present. It collects data on patient age, sex, zip code, billed charges, codes for diagnoses and procedures, and other relevant variables. Through our linkage with the objective indicators of diagnosis, morbidity, and treatment history in the Comprehensive Hospital Abstract Reporting System, we can confirm self-reported diagnoses and compare them with other variables of interest obtained from registry surveys. This approach is well suited to studies of the clinical severity and outcomes of illnesses and health conditions in member twins. Given a sufficiently large number of matches between the registry and this reporting system, these data will enable estimates of the genetic and environmental contributions

to critical health outcomes requiring hospital care. We will also be able to target recruitment for future epigenetic and other laboratory studies to twin pairs whose morbidity and treatment histories are verified.

### Geocoding and Built Environment Data

Over the past 3 years, UW Twin Registry investigators have geocoded more than 18,000 individual records of street addresses reported by member twins in various surveys. Since members sometimes move from one location to another, the number of addresses substantially exceeds the number of registry members. Geocoded addresses are then coupled with objective environmental data that have been integrated and are available in geospatial information system databases for large geographic areas, including all but four counties in Washington State. This process continues for each new survey conducted by the registry and each new address reported over time.

Based on these data, we have developed several variables relevant to built and social environmental exposures, including neighborhood walkability scores for 4,957 pairs, derived from a commercially available algorithm; walkability indices for 1,375 pairs, constructed from measures of urban form and utilitarian destinations; Singh indices for 3,339 pairs, which provide measures of social deprivation (Singh, 2003); and median household income for 3,339 pairs, computed for census block group as well as tract level. We have also developed exposure variables based on the Uniform Crime Report to derive a crime index, and we have created a County Sprawl Index and a Normalized Difference Vegetation Index (exposure to green spaces). With these rich resources, we can use existing survey data and our newly developed exposure variables to conduct multi-level analyses, and we can recruit twins for in-person studies to obtain more sophisticated, objective measures of behavior, health, and environment.

## Collaborative Research

### Scope

Although the UW faculty who originally developed and currently maintain the UW Twin Registry have continued to use its resources for an impressive series of scientific investigations, the registry's primary purpose is to encourage new collaborations with investigators across the United States and around the world. To date, researchers have used the registry to obtain competitive funding from the NIH and private foundations for studies ranging from infectious disease to chronic pain. From the NIH, investigators working with registry data have obtained five R01 awards and three K awards, as well as various R03, R21, R55/56, RC2, P01, P60, U01, and U54-sponsored grants. Sponsors have included the National Heart, Lung and Blood Institute, the National Institute of Arthritis and Musculoskeletal and Skin Diseases, the National Cancer Institute, the National

Institute of Diabetes and Digestive and Kidney Diseases, the National Institute of Child Health and Human Development, the National Institute of Nursing Research, and the National Institute on Aging. Investigators currently associated with the Registry are based at institutions across the United States, including Kentucky, Louisiana, Missouri, New Jersey, New York, and Virginia, as well as at other twin registries worldwide.

Much recent twin research focuses on epigenetic mechanisms and gene-by-environment interactions in various phenotypes of interest. The UW Twin Registry is extremely well placed to assist this work, given the richness and diversity of its data and the range of strategies that have been developed and optimized to recruit twins for in-person studies. Investigations with registry participants have been successful even when they used intensive protocols that required precise quality control, at-home collection of survey and biospecimen data, and in-person visits or overnight hospital stays involving blood draws, fasting, evoked pain stimuli, brain imaging, or measures of exercise physiology.

### Structure and Process

The leadership of the UW Twin Registry consists of four faculty members who hold the titles of Director, Associate Director, Research Director, and Associate Research Director. Our professional staff includes a Scientific Operations Manager along with several research coordinators and assistants. Investigators who wish to work with the UW Twin Registry typically proceed in three steps. The first step is initial contact with the leadership team, usually the Associate Director or Scientific Operations Manager. Initial conversations cover the proposed scope of the collaboration and any preliminary data that would support the investigation. When preliminary data are available, they are typically analyzed for use in a manuscript or as preliminary findings for a grant application. In either case, the second step is that the investigator submits a brief research application for review by the Registry Directors. If approved, the project progresses to its third step: grant submission and funding. At least one faculty member associated with the registry is typically a collaborator on any projects that use registry data. Member contact information is not released to investigators until members confirm a potential interest in the project. Initial contact with Registry members for any study must be made by registry personnel.

In addition to study-specific costs, collaborating investigators are charged a fee by the registry cost center to help sustain the infrastructure required to keep the registry running. Fees can be assessed for access to registry-wide data for new analyses, contact information for mailing surveys, biospecimens (assessed per twin pair), and enrolling members in in-person studies (again assessed per twin pair). Fees are based on infrastructure costs and projected usage for the fiscal year. As infrastructure costs are relatively stable, wider usage of the registry reduces fees for all investigators.

## Future Directions

The research priorities of many funding bodies include genetics, epigenetics, gene-by-environment interactions, and the various omics. The study of twins, especially twin pairs who are discordant for a phenotype of interest, is one of the most efficient and effective ways to investigate critical areas of health and disease (MacGregor et al., 2000; van Dongen et al., 2012). The size and scope of the UW Twin Registry makes it one of the few large twin registries in North America that can investigate a broad range of scientific questions. For example, registry researchers are currently studying the influence of sleep duration on DNA methylation, with future studies focused on assessing concomitant gene expression patterns from RNA derived from peripheral blood leukocytes. The primary focus of the registry over the next 5 years will be to establish new collaborations with investigators around the world, and to contribute to consortia that can take advantage of our extensive holdings of biospecimens, survey data, and clinical data, along with their fruitful linkage to an array of local and national health databases.

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