

The Mid-Atlantic Twin Registry, Revisited

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The Mid-Atlantic Twin Registry (MATR) is a population-based registry of more than 56,000 twins primarily born or living in Virginia, North Carolina, and South Carolina. The MATR employs several methods of ascertaining twins, and devotes considerable resources to tracking and maintaining communication with MATR participants. Researchers may utilize the MATR for administration of research services including study recruitment, collection of DNA, archival data set creation, as well as data collection through mailed, phone, or online surveys. In addition, the MATR houses the MATR Repository, with over 1,200 blood samples available for researchers interested in DNA genotyping. For over 35 years MATR twins have participated in research studies with investigators from diverse scientific disciplines and various institutions. These studies, which have resulted in numerous publications, have covered a range of topics, including the human microbiome, developmental psychopathology, depression, anxiety, substance use, epigenetics of aging, children of twins, pre-term birth, social attitudes, seizures, eating disorders, as well as sleep homeostasis. Researchers interested in utilizing twins are encouraged to contact the MATR to discuss potential research opportunities.

■ **Keywords:** twin, registry, genetics, repository, recruitment

History and Summary

The Mid-Atlantic Twin Registry (MATR) is a population-based registry of twins and their families that was formed through the convergence of the Virginia Twin Registry (est. circa 1975) and the North Carolina twin registry in 1997 and the addition of South Carolina in 1998. To date, the number of registered twins ('participants') in the MATR totals more than 56,000, with nearly 50,000 of these individuals representing complete twin pairs of same- and opposite-sex twins (see Tables 1 and 2 for more information). These participants have been drawn primarily from the more than 210,000 identical and fraternal twins born in these three states between 1913 and 2010, although twins from all over the United States may join. The MATR is located administratively under the Vice President for Research in the Office of Research at Virginia Commonwealth University (VCU). The MATR does not conduct its own research, but facilitates twin studies for researchers from a myriad of disciplines. Researchers may utilize the MATR for administration of research services, including study recruitment, collection of DNA, archival data set creation, as well as data collection through mailed, phone, or online surveys. Over the years, MATR twins and their family members have participated in numerous research projects for subsidiary studies (see Publications and Citations) and for the MATR's data and sample collection efforts (see Research Resources).

Methods

Twin Ascertainment

The MATR's primary source of twin ascertainment is through birth records obtained from Virginia, North Carolina, and South Carolina. In previous years, the MATR also conducted school recruitment to ascertain juvenile twin pairs. These methods are described in further detail elsewhere (Anderson et al., 2002).

The MATR's home university of VCU is also home to one of the largest academic medical centers in Virginia, the VCU Health Systems (VCUHS). Recently, the MATR partnered with the VCUHS to implement two methods for ascertainment of twins who visit VCUHS clinics as patients. The first method is implemented by VCUHS hospital call centers, which collect multiplicity data during the patient's scheduling phone call by asking if they are a twin. If so, they then obtain the twin's permission to provide their contact information to the MATR. The second method involves placement of MATR registration brochures

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TABLE 1
Twins and Multiples Registered in the MATR by Msex and Age Group

| Pair/multiple sex (msex) | Age groups | | | | | Total |
|--------------------------|---------------|---------------|----------------|----------------|---------------|-----------------|
| | 00–18 | 18–25 | 26–40 | 41–65 | 66+ | |
| FF | 2,306 (4.60) | 3,164 (6.31) | 5,436 (10.84) | 4,696 (9.36) | 2,264 (4.51) | 17,866 (35.63) |
| FFF | 12 (0.02) | 0 (0.00) | 3 (0.01) | 35 (0.07) | 9 (0.02) | 59 (0.12) |
| FFFF | 0 (0.00) | 0 (0.00) | 0 (0.00) | 3 (0.01) | 0 (0.00) | 3 (0.01) |
| MF | 1,644 (3.28) | 2,422 (4.83) | 3,248 (6.48) | 4,134 (8.24) | 2,744 (5.47) | 14,192 (28.30) |
| MFF | 15 (0.03) | 5 (0.01) | 9 (0.02) | 8 (0.02) | 17 (0.03) | 54 (0.11) |
| MFFF | 0 (0.00) | 4 (0.01) | 0 (0.00) | 0 (0.00) | 0 (0.00) | 4 (0.01) |
| MM | 2,122 (4.23) | 3,044 (6.07) | 4,582 (9.14) | 4,532 (9.04) | 3,512 (7.00) | 17,792 (35.48) |
| MMF | 11 (0.02) | 3 (0.01) | 12 (0.02) | 44 (0.09) | 17 (0.03) | 87 (0.17) |
| MMFF | 0 (0.00) | 0 (0.00) | 0 (0.00) | 4 (0.01) | 0 (0.00) | 4 (0.01) |
| MMM | 12 (0.02) | 3 (0.01) | 3 (0.01) | 23 (0.05) | 5 (0.01) | 46 (0.09) |
| Unknown | 2 (0.00) | 4 (0.01) | 30 (0.06) | 2 (0.00) | 2 (0.00) | 40 (0.08) |
| Total | 6,124 (12.21) | 8,649 (17.25) | 13,323 (26.57) | 13,481 (26.88) | 8,570 (17.09) | 50,147 (100.00) |

Note: Numbers given as frequency (percent). M = Male, F = Female.

TABLE 2
Twins and Multiples Registered in the MATR by Race

| Race | Freq & (Pct) |
|----------------------------|----------------|
| Asian or Pacific Islander | 154 (0.31) |
| African American | 6,234 (12.43) |
| Hispanic | 199 (0.40) |
| American Indian or Alaskan | 128 (0.26) |
| Mixed Race | 62 (0.12) |
| Other | 459 (0.92) |
| Unknown | 3,747 (7.47) |
| Caucasian | 39,164 (78.10) |
| Total | 50,147 |

Note: Freq = frequency; Pct = percent.

at VCUHS hospital clinics, which twins or parents of twins can complete to become registered.

In 2010, VCU received a Clinical & Translational Science Award (CTSA), supporting the progress of interdisciplinary research, networking, and community involvement. As part of the CTSA consortium, the MATR has access to CTSA initiatives for research subject recruitment, such as ResearchMatch (www.researchmatch.org). Through ResearchMatch, the MATR can search for twins and higher-order multiples in the community and invite them to become involved in twin-related research.

Registration

Prior to participation in MATR studies, twins and/or their families must first register in the MATR. Adult twins (ages 18 and older) can register individually. Juvenile twin pairs (age 17 and younger) must be registered by their parents or legal guardian. Registration involves collecting demographic and contact information as well as asking a series of zygosity questions. In order to register participants, the MATR typically mails a registration packet to the adult twin or parent/legal guardian of juvenile twins. The packet includes a letter with information about the MATR, the MATR Privacy Policy, a recent newsletter, their rights as a research participant, a scannable registration form, and a postage-free return envelope. The enclosed letter also describes how

the twin or parent of twins can register with the MATR online. If no response is received within 2–4 weeks after sending the packet, MATR research interviewers follow-up via phone. During the phone call, the interviewers provide the twin or parent/legal guardian of twins with information about the MATR and invite them to register. Some twins and their families may discover the MATR through various sources such as the Internet, word of mouth, or through an outreach event (see Events) and are also welcome to join the MATR. These twins can register in person at an event, request a mailed packet or phone call, or may simply register online through the MATR registration Web survey.

Study Recruitment

Once registered in the MATR, participants are eligible to receive invitations for research studies. The majority of our studies contact twins via phone, for which the MATR employs a series of points of contact. This includes sending an introductory letter prior to calling a twin, which includes a brief overview of the study and alerts the twin to anticipate a phone invitation for the study. Enclosed with this introductory letter is a form to collect current contact information and a postage-free envelope, enabling the twin to easily update the MATR with their information. One week after this letter is sent, MATR interviewers begin calling the twin. If the interview is not completed after approximately seven phone calls, the MATR sends a ‘Trying to Reach You’ letter to the twin, which encourages them to return the call or answer the phone and let the interviewer know whether or not they are interested in the study.

Zygosity Determination

During registration, twin zygosity is determined through a physical similarities questionnaire based on Nichols and Bilbro (1966). Many subsidiary studies that collect DNA for genotyping purposes, also conduct DNA zygosity testing. After obtaining consent from both twins, the results of the tests are returned to the MATR for record keeping. The manner of data collection and the zygosity determination

are tracked and updated if more confident data is collected for the twin pair. For instance, once DNA testing results are obtained, this is kept on record as the source of zygosity rather than questionnaire determination.

Tracking Twins and Twin Families

The MATR uses a variety of public and private resources to obtain current contact information for twins and their families. Given the frequency with which the US population moves, maintaining current contact information for participants is vital to the success of the registry. Sources used by the MATR for tracking twins include address matching with the state departments of motor vehicles (in states where such access is permissible) or through matches with the National Change of Address database with the US Post Office. The MATR also utilizes various privately managed, nation-wide search databases, which pull information from a variety of sources such as credit header information and public records.

In addition to tracking twins through these sources, the MATR encourages twins to proactively update their contact information by phone, email, or completing an online form. This allows twins to provide their current contact information in a convenient manner to ensure continued communication as well as conserving valuable resources, which would otherwise be spent tracking MATR participants.

During most points of contact, participants are asked to provide the name of a person that the MATR may keep on record and call to obtain current contact information about the participant. This person is contacted if the participant is difficult to locate through other methods.

Research Resources

MATR Repository

In addition to the registry, the MATR is cultivating a repository, which currently consists of blood samples from more than 1,200 twins, with over 800 of those samples representing complete pairs. These samples are available for researchers looking to conduct DNA extraction for a range of genomic analysis. Twins who provided blood samples also consented for the MATR to connect their sample with their previously collected phenotypic data, such as developmental data on a number of psychiatrically relevant phenotypes. In doing so, the MATR can facilitate researcher collaboration for extensive psychiatric and genomic analyses. The VCU laboratory housing the MATR Repository is available to provide a variety of services. Interested researchers may contact the MATR Administrator or Scientific Director for access to this resource.

MATR Adult Health Surveys

The MATR collects and stores health and behavior data from adult twins in order to screen and select participants

for research studies targeting twins with specific diseases or other characteristics. These data are available for researchers interested in conducting archival data analysis.

Adult Health and Personality (AHP). The AHP survey was administered from 1999 to 2002 with 3,882 adult participants, and over 1,200 of those individuals representing complete pairs. This survey contained questions regarding height, weight, personality attributes, depression, alcohol and tobacco use, major diseases and conditions, and number of offspring.

Online MATR Adult Survey (MAS). In the winter of 2011, the MATR initiated an online MAS for adult twins. The MAS collects information similar to the AHP survey, as well as additional diseases, conditions, attitudes, behaviors, and information about substance use. The Web-based platform provides a cost-effective and immediate method of data collection by streamlining the data directly from participant to the MATR database. Data collection efforts are ongoing with a goal of inviting all registered, adult twin participants to take part.

Twin Communications and Outreach

Twin Matters Newsletter

Maintaining contact with our participants is an integral part of the registry. The MATR produces a biannual newsletter, *Twin Matters*, for twins and their families, as one method of continued contact with participants. The newsletters include twin stories, study announcements and updates, as well as articles of interest to twins. Advertisements for research studies are also included in the MATR newsletter, following Institutional Review Board (IRB) approval.

Events

The MATR annually partners with Cedar Faire Entertainment Company to co-host Multiples Family Day at two of their amusement parks, Kings Dominion in Virginia, and Carowinds on North Carolina/South Carolina border. Twins are offered discounted admission tickets to the amusement parks where they can socialize with fellow twins as well as the MATR staff and take part in twin-centric contests. In addition, the MATR attends several events a year in efforts to raise name recognition, awareness of twin research, and for registration of new members. This includes twin-specific events such as regional or local Mothers of Multiples club gathering or public events such as health fairs and expos.

On the Web

The MATR Web site provides information for twins as well as researchers. Twins can learn more about the MATR, twin research, current studies, and can read articles about common questions pertaining to twins. Researchers can find information about recent publications, MATR services, and

statistics about MATR participants. In addition, the MATR is developing a presence on social media sites by working with VCU marketing to reach out to the VCU community through Facebook and Twitter.

MATR Administration and Research

The MATR is an active human subjects protocol at VCU, which is overseen by the VCU IRB and undergoes annual review. Protecting the confidentiality and privacy of participants is of utmost importance, and the MATR employs many electronic and physical safeguards to do so, including firewalled computers, encrypted data servers, and microchip office entry. In addition, all MATR employees undergo training in human subjects protection and MATR Standard Operating Procedures, sign confidentiality agreements, and are only privy to the least amount of information needed for them to perform their jobs.

The MATR is overseen by the Scientific Director and the Financial Director who periodically meet with the MATR Scientific Advisory Committee. The Advisory Committee and Directors steer the MATR toward advantageous initiatives and review applications from researchers who wish to access MATR twins for their study. The MATR welcomes researchers from all institutions and fields of study to utilize the MATR in order to fulfill their twin-related research goals. Interested researchers may visit www.matr.vcu.edu for information on the application process and how to contact the MATR Administrator or Scientific Director.

Services

Researchers utilize the MATR for a variety of services including:

- placing study advertisements in the MATR newsletter
- creating archival data sets
- matching data from various public and private resources
- sending mailed questionnaires
- creating online surveys
- conducting telephone surveys/screenings
- orchestrating in-home interviews
- coordinating participant recruitment
- facilitating researcher networking
- collecting DNA samples (blood, saliva)

The MATR provides many years of experience in project planning and design as well as study management, such as document creation and interacting with VCU IRB.

Publications and Citations

In addition to those listed in the 2002 article about the MATR (Anderson et al., 2002), the MATR has worked with investigators and collaborators from such institutions as

VCU, Duke University, University of Pennsylvania School of Medicine, National Institute of Child Health and Development, National Institute of Drug Abuse, National Institute of Environmental Health Sciences, New York University, and Columbia University. Published articles arising from studies that utilized MATR twins include such topics as adult depression (Kendler & Halberstadt, 2012), developmental psychopathology (Eaves et al., 2010; Prom-Wormley et al., 2009), children of twins (Silberg et al., 2010, 2012), substance use (Chen et al., 2009; Gillespie et al., 2009; Kendler et al., 2011; Maes et al., 2011), anxiety in adults (Hettema et al., 2012), pre-term birth (York et al., 2010), social attitudes (Eaves & Hatemi, 2008; Verhulst et al., 2012), seizures (Corey et al., 2011), eating disorders (Mazzeo et al., 2010, Mitchell et al., 2010), sleep (Gehrman et al., 2011), and chromosomal changes (Jones et al., 2012). Additional recent study topics include the human vaginal microbiome, sleep homeostasis, epigenetics of aging, socio-political attitudes, genome-wide association studies (GWAS) of substance use, development of anxiety in juveniles, as well as rheumatoid arthritis and the intestinal microbiome. The MATR has also created de-identified data sets for researchers by matching MATR records with the Department of Vital Statistics, the VA Department of Motor Vehicles, and the Virginia Cancer Registry.

In publications, MATR twins may be cited under names of previous studies such as: the Virginia Twin Registry, the Virginia Twin Study of Adolescent Behavioral Development, the Children of Twins Study, the Young Adult Follow Up, the Virginia 30,000, and the Virginia Adult Twin Study of Psychiatric and Substance Use Disorders.

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