

The Mid-Atlantic Twin Registry

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The Mid-Atlantic Twin Registry (MATR) is a population-based registry of twin pairs ascertained from birth records and school system records of Virginia, North Carolina, and South Carolina. The MATR was formed in 1997 with the merging of the Virginia and North Carolina Twin Registries, and it expanded to include South Carolina when access to twin birth records in that state was granted in 1998. Registered twins ("participants") number more than 51,000, with approximately 46,000 of these individuals representing complete pairs. Roughly two-thirds of MATR participants are over age 18, with a mean age of approximately 35 years. These participants have primarily been drawn from the more than 170,000 identical and fraternal twin pairs born in the three states between 1913 and 2000. Twins and their family members have participated in numerous research projects, ranging from general health surveys to studies on specific health topics such as cardiovascular disease; depression and anxiety; seizures; behavioral development; pregnancy complications; conduct disorder; drug use, abuse, and dependence; cleft lip/palate; obesity; and chronic fatigue syndrome. The MATR has established a privacy policy and strict standard operating procedures to protect the confidentiality of participant data. The MATR considers a limited number of qualified requests per year from investigators interested in recruiting MATR participants into their research studies.

The Mid-Atlantic Twin Registry is a population-based registry of twins born in or living in Virginia, North Carolina, and South Carolina and is located in the Virginia Institute for Psychiatric and Behavioral Genetics, Department of Human Genetics, at Virginia Commonwealth University (VCU). Registered twins ("participants") number more than 51,000, with approximately 46,000 of these individuals representing complete pairs. These participants have been drawn primarily from the more than 170,000 identical and fraternal twin pairs born in the three states between 1913 and 2000. Twins and their family members have participated in numerous research projects, ranging from general health surveys to studies on specific health topics such as cardiovascular disease, depression and anxiety, seizures, behavioral development, pregnancy complications, conduct disorder, substance use and abuse, cleft lip/palate, obesity, and chronic fatigue syndrome. These projects have been conducted by researchers from VCU, the MATR's home, and from institutions around the world.

Methods

Identification

The MATR has obtained records of multiple births from 1915 to 2000 in Virginia (VA), 1913 to 2000 in North Carolina (NC), and 1915 to 2000 in South Carolina

(SC). Permission to access these records was granted by state vital records offices in 1978 (VA), 1990 (NC), and 1998 (SC). From these records, the MATR has identified more than 170,000 twin births. The MATR annually obtains records of multiple births for the prior birth year from each state. Currently, an estimated 2,800 twin births occur each year in the three states combined, which together have a total estimated population of about 19 million (Table 1). On a periodic basis, the MATR requests from the school systems in the three states their assistance in identifying juvenile twins enrolled in their schools. SC Public Schools participated in such an effort in 2000 (Table 2).

The MATR uses a variety of public and private resources to obtain current contact information for twins identified through birth records. For twin births occurring within the past 1–2 years, the address on the birth records is likely to be sufficient to locate the family. In the case of juvenile twins aged 3–17, the MATR may seek the parents' current contact information by matching address information from the birth certificate with contact information held by state departments of motor vehicles (in states where such access is permissible) or through matches with various privately managed, nationwide databases. These databases access sources such as credit header information derived from the three major U.S. credit bureaus; public records from some states, such as voter registration records or department of motor vehicle records; and consumer information such as warranty registration data. Two approaches are used in seeking twins' current contact information: electronic batch matching or a more intensive "caseworker" search. In electronic batch matching, 1000 or more records may be processed for a match at one time, and an algorithm is used to determine whether a given twin record matches available address data. This method may produce more than one candidate match for a record and is economical for records on which recent, valid address information is available. In the caseworker method, an experienced "tracer" uses results from electronic batch matching and additional proprietary sources to select the most likely candidate for a match. The tracer may contact the candidate match to confirm his or her identity. This method, while more costly than batch matching, is appropriate for twins ascertained from birth

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Table 1
Twin Births in VA, NC, SC

	VA	NC	SC	Total
Estimated population (2000)*	7,078,515	8,049,313	4,012,012	19,139,840
Twin birth rate per 100 births	1.37	1.42	1.35	1.38
Estimated twin births/year	1000	1250	600	2850
Twin births ascertained, c. 1915–1999	55,341	64,288	51,740	171,369

Note: *From U.S. 2000 Census

Table 2
School-based Ascertainment Efforts

State	Year	Percent of participating districts	Approximate pairs ascertained
VA	1985	95	5000
NC	1993	92	5500
SC	2000	92	4000

records prior to circa 1970, on which outdated, limited, or no past address is available.

Recruitment

The MATR mails invitations to register to candidate adult twins or the parents of juvenile twins. The registration packet contains a cover letter, an optically scannable registration form, a statement of MATR participants’ rights and the MATR’s responsibilities to participants, and a color brochure describing the MATR. The registration form collects basic demographic data such as contact information, ethnicity, number of non-twin siblings, number of children (asked of adult twins), and a standard series of questions designed to determine zygosity with greater than 97% accuracy (Magnus et al., 1983). The act of registration means that the twin (or parent of juvenile twins) gives the MATR permission to contact her/him with invitations to participate in research or with information of interest to twins, such as the MATR’s biannual newsletter (which contains research summaries and twin stories and facts) or announcements about twin events. Completed registration forms are scanned into a data file. The MATR conducts telephone follow-up with non-responders.

Data Collection

Twins must be registered in the MATR before any further data collection can take place. The MATR administers periodic (biennial) health surveys to adult participants and health and development surveys to parents of juvenile twins, particularly those of preschool age. For adult twins, the surveys facilitate data screening to identify twins eligible for specific studies. Because of their use as screening tools, substantive aspects of these surveys may vary to accommodate upcoming studies. Some core topics, such as personal and family health history, height and weight, and smoking and drinking history, are common to most adult surveys. Three juvenile health and development surveys have been designed to follow twins from preschool age through early primary school years, and are administered at ages 18–35 months,

3–5 years, and 6 and older. These surveys are conducted primarily to collect longitudinal information on developmental variables and secondarily for screening purposes.

In general, mailings may be preceded 10 days to 3 weeks by a “heads-up” postcard to alert recipients of the impending registration packet or survey. A reminder/thank-you card typically is sent 10–15 days after the first mailing of a registration packet or survey, followed by a second mailing to non-responders within 4–6 weeks of the date of the first mailing. All mailed items request postal return service to provide the MATR with address updates or the knowledge of no available address for participants who have moved without notifying the MATR. The MATR’s team of trained interviewers conducts telephone follow-up for registration and survey efforts. When telephone follow-up is employed, the second mailing to non-responders typically is omitted from the process. However, a small proportion of those contacted by telephone request that the registration packet or survey be mailed to them a second time, generating the need to process re-mails in smaller batches.

MATR Composition

The MATR currently consists of more than 51,000 registered individual twins of all ages, of which approximately 46,000 represent living, complete pairs. Ages range from less than one to 85 years, with a mean age of about 35; approximately 66% of twins are 18 or older. Tables 3–5 include information on the composition of the MATR. Roughly 46% of MATR participants were born in VA, 44% in NC, and 3% in SC, where, to date, little recruitment activity has occurred. The majority of these twins have registered by mail, which until 2002 was the MATR’s primary recruitment medium. Fewer than 5% of the registrations that occur in the MATR are self-initiated. Candidate participants initiate this process by mail, email, or telephone.

The activities of the MATR’s predecessor registries account primarily for the current composition of the registry. The VA Twin Registry (VTR; 1978–1996) focused

Table 3

Twins by Age Group and Pair Sex

Age Group	FF	MM	MF	Total
Complete pairs <i>N</i> (%)				
Newborn–5	655 (7.6)	642 (9.2)	550 (7.2)	1847 (8.0)
6–12	1398 (16.5)	1214 (17.4)	947 (12.4)	3559 (15.4)
13–17	635 (7.5)	594 (8.5)	456 (5.9)	1685 (7.3)
18–25	984 (11.6)	729 (10.5)	564 (7.3)	2277 (9.8)
26–35	1254 (14.8)	795 (11.4)	1038 (13.5)	3087 (13.4)
36–45	1523 (18.1)	1022 (14.6)	1487 (19.4)	4032 (17.5)
46–55	1204 (14.3)	913 (13.1)	1237 (16.2)	3354 (14.5)
56–65	411 (4.9)	526 (7.5)	651 (8.4)	1588 (6.9)
66 and older	385 (4.7)	543 (7.8)	744 (9.7)	1672 (7.2)
Total	8449 (36.6)	6978 (30.2)	7674 (33.2)	23,101
Incomplete pairs <i>N</i> (%)				
18–25	127 (10.9)	88 (4.0)	101 (4.8)	316 (5.8)
26–35	282 (24.2)	317 (14.4)	387 (18.2)	986 (18.0)
36–45	386 (33.2)	502 (22.9)	552 (26.0)	1440 (26.3)
46–55	239 (20.5)	486 (22.2)	479 (22.6)	1204 (22.0)
56–65	67 (5.8)	281 (12.8)	230 (10.8)	578 (10.5)
66 and older	63 (5.4)	521 (23.7)	374 (17.6)	958 (17.5)
Total	1164 (21.2)	2195 (40.0)	2123 (38.7)	5482

Table 4

Twins by Zygosity and Pair Sex

Age Group	FF	MM	MF	Total
Complete pairs <i>N</i> (%)				
DZ	1941 (8.4)	1983 (8.6)	7674 (33.2)	11,595 (50.2)
MZ	2223 (9.6)	2118 (9.2)	—	4341 (18.8)
Undetermined*	4285 (18.6)	2877 (12.5)	—	7165 (31.0)
Total	8449	6978	7674	23,101
Incomplete pairs <i>N</i> (%)				
DZ	459 (8.3)	924 (16.9)	2123 (38.7)	3504 (63.9)
MZ	415 (7.7)	799 (14.5)	—	1214 (22.2)
Undetermined*	290 (5.2)	472 (8.6)	—	764 (13.9)
Total	1164 (21.2)	2195 (40.0)	2123 (38.7)	5482

Note: *Data available but not yet analyzed.

Table 5

Twins by Ethnicity and Pair Sex

Age Group	FF	MM	MF	Total
Complete pairs <i>N</i> (%)				
Caucasian	6448 (27.9)	5412 (23.4)	5538 (24.0)	17,398 (75.3)
Black	1259 (5.5)	873 (3.8)	989 (4.3)	3121 (13.5)
Other	156 (—)	140 (—)	101 (—)	397 (1.7)
Unreported	586 (2.5)	553 (2.4)	1046 (4.5)	2185 (9.5)
Total	8449	6978	7674	23101
Incomplete pairs <i>N</i> (%)				
Caucasian	829 (15.1)	1702 (31.1)	1333 (24.3)	3864 (70.5)
Black	267 (4.9)	429 (7.8)	492 (9.0)	1188 (21.7)
Other	17 (—)	23 (—)	29 (—)	69 (1.2)
Unreported	51 (1.0)	41 (1.0)	269 (4.9)	361 (6.6)
Total	1164 (21.2)	2195 (40.0)	2123 (38.7)	5482

recruitment primarily on adult twins until 1995. The NC Twin Registry (1990–1996) recruited twins of all ages. Since 1999, the MATR has launched three large-scale efforts to recruit new juvenile twins. These included its first attempts to recruit preschool and school-aged twins in SC. In 2002, the MATR has focused on recruitment of adult twins to fulfill the needs of several new research projects. With the exception of a project in the 1980s to recruit a volunteer sample of elderly twins by advertising in a newsletter of the American Association of Retired Persons (AARP), VCU researchers acting on behalf of the MATR have not targeted any specific cohort for extensive recruitment. The AARP project, which was conducted along with VTR recruitment efforts, resulted in more than 9000 individual twins aged 55 or older taking part in one or more surveys on topics such as health and lifestyle, personality, and habits and opinions (Eaves et al., 1997, 1999). The majority of these twins have not been contacted for 5–10 years; therefore, their data are not included in the official reports of MATR composition. A pilot project to re-establish contact with and survey these individuals was initiated in 2002.

Data Collection

The MATR has collected basic health data and family health history data from adults since the early 1980s with the advent of the VTR. More than 24,000 adult twins have completed at least one basic health survey. This number includes both members of 8408 complete registered pairs and one member of 2389 complete registered pairs. Of the incomplete registered adult pairs, 4879 individuals have provided health data. Parents of nearly 2500 juvenile twin pairs have completed at least one health and development survey. The MATR also has access to neonatal data collected on birth certificates. This information is particularly rich (approximately 75 variables) for twin pairs born after 1990. The MATR has identified 36,677 birth certificates containing some neonatal data, and 4820 pairs from this group are registered. Of these 4820 pairs, the parents of 2246 have completed at least one health survey.

Research

From the inception of the VTR to the present-day MATR, more than 300 scholarly papers based on data from MATR participants have been published in refereed journals. Many have been landmark papers in their discipline. Study topics have included seizures and epilepsy (Corey et al., 1991, 1998), eating disorders (Bulik et al., 1998; 2000), major depression (Kendler & Prescott, 1999), anxiety and depression (Silberg et al., 2001; Silberg et al., 1999), substance use and abuse in adults (Heath et al., 1991; Kendler et al., 2000; Prescott et al., 1994, 2000; Prescott & Kendler, 2001) and adolescents (Bulik et al., 2001; D'Onofrio et al., 1999; Maes et al., 1999), general mental health and illness (Kendler et al., 2000; Kendler, 2001; Sullivan & Kendler, 1998), cardiovascular disease (Schieken et al., 1989; van den Bree et al., 1996), religiosity (Truett et al., 1994), adolescent behavioral development (Eaves et al., 1997), and obesity (Maes et al., 1997).

Current Research Focus

Current research projects favor, but are not limited to, psychiatric and behavioral topics. These include an epidemiological study of chronic fatigue syndrome, a family study of depression and disruptive behavior in children of twins, a study of the transition from tobacco use to dependence in young adults, a study of anxiety and substance use/abuse, and a study of female twin pairs discordant for either depression or alcohol use. Other topics include the genetic epidemiology of seizures, polycystic ovary syndrome, and rheumatoid arthritis. Investigators and collaborators represent institutions such as VCU, Veterans Affairs Hospitals, Duke University, Emory University, the University of Washington, the University of Oslo, the Southern University of Denmark, the University of North Carolina — Chapel Hill, and the Institute of Psychiatry — London.

Legal and Ethical Issues — Privacy and Confidentiality

The MATR has implemented numerous procedures to protect the privacy of research participants. Because the data from twin research participants represents a major resource for researchers in genetics as well as other fields, many researchers seek twins for different types of projects. The increasing demand for twins, combined with the increasing information-related concerns of modern Western culture, have created challenges related to MATR participant privacy as well as protection of raw data. Hence, the MATR takes a number of steps to ensure data confidentiality and the privacy of its participants. These include an IRB-approved privacy policy and standard operating procedures, both designed to safeguard data confidentiality in daily operations. The MATR also works with privacy consultants as needed to proactively resolve privacy-related issues. For example, privacy consultants recently conducted a review to ensure that standard procedures of daily MATR operations adequately protected participant privacy and confidentiality in accordance with national standards.

The MATR's IRB-approved privacy policy describes how the MATR collects and stores participant data and dictates which persons (including participants) are authorized to access those data. The MATR will not allow researchers to contact a participant unless the MATR first obtains the participant's permission. Data access rights are extended only to the individual on whom the information is held (in the case of a minor, her/his parent or legal guardian also). MATR employees access participant data only to the level necessary to complete an authorized task. MATR employees receive training in privacy and confidentiality issues, sign confidentiality agreements, and, as Virginia state employees, undergo background checks. Agents conducting work for the MATR must sign service provider confidentiality agreements and adhere to certain procedures designed to protect the interests of MATR participants and the MATR itself.

The MATR developed more than 80 IRB-approved, standard operating procedures (SOPs) for daily operations. SOPs include instructions for safeguarding data and

protecting participants' privacy. Key to maintaining data confidentiality is the location of the MATR data servers in an electronically and physically secured suite with limited employee access. The data servers are inaccessible by Internet. Participants' personally identifiable information (PII) (e.g., name, address) is stored on a server separate from the server storing other data (e.g., health data) that participants provide. Passwords are required to access any database. PII on hard copy is destroyed (e.g., shredded) when no longer needed. Participant data collected via survey is optically scanned. After verification of the scanned data, any hard copy surveys are destroyed, and the electronic data are filed on CD-ROM and stored in fire-safe vaults. When the MATR provides data sets to researchers approved to access the MATR, the participant ID numbers are encrypted such that the ID numbers in the data set cannot be linked to ID numbers in the MATR data system.

Special Features

Researcher Access

The MATR considers a limited number of proposals each year from researchers interested in accessing MATR participants to conduct specific studies. Administrative fees and labor costs are charged according to the scope of the project. Interested researchers must submit a letter of intent describing the proposed research protocol to the MATR Director, who reviews the letter with other members on the MATR Executive Committee. If the proposal appears feasible, the researcher is invited to meet with the Executive Committee. If both parties agree to proceed, the proposal undergoes a more formal review by an advisory committee, during which the project's compelling need for twins, scientific merit, and participant burden, among other issues, are considered. Approved proposals are granted access and scheduled for implementation. Principal investigators sign a researcher agreement before beginning the project. They agree to abide by the NATR SOPs, provide annual progress reports to the MATR, provide the MATR with any updated participant contact data they collect during the project, and return or destroy all participant PII at the conclusion of the data collection phase of the project.

Participant Communication

The MATR encourages participant input and feedback. To this end, the MATR publishes a biannual, full-color newsletter that summarizes ongoing research efforts and includes information of interest to twins; maintains a website with resources for twins and a mechanism for contacting the MATR by email; and operates a 24-hour toll-free line on which participants may leave messages.

The MATR has recognized the need for a liaison for MATR participants and has established the position of Participant Coordinator (PC), which is staffed as funding allows. The role of the PC is to co-design, supervise, and facilitate successful and harmless interactions between MATR participants and MATR-related researchers and other staff and to ensure ethically sound treatment of MATR participants by MATR-related agents. This role requires an attentive balance between MATR public relations, ethical treatment of MATR participants, and

competent adherence to research protocols. A large part of the PC's role involves maintaining communication links between the PC (as a representative of MATR participants), MATR staff such as research interviewers, and investigators accessing MATR participants for their research. Key to this communication network is responding effectively to all MATR email/postal mail and calls on the MATR's toll-free line.

The MATR receives more than 125 participant inquiries per month, roughly half of which are generated by interviewer calls to collect data. The purpose of participant-initiated contact often is as simple as providing an address update or returning a call from a MATR interviewer to complete a telephone survey. More complex participant inquiries involve: (1) questions about certain medically-related or social traits as experienced by twins and/or their families; (2) requests for information about the MATR (e.g., how to register); (3) queries regarding certain study protocols including substantive questions about study objectives; and (4) complaints related to MATR activities and/or requests by MATR participants to be removed from the registry (Table 6).

Future Plans

In the future, the MATR plans to conduct more targeted recruitment efforts by seeking new participants who appear eligible for upcoming studies. In contrast with some past effort to recruit twins of all ages, this approach most efficiently uses available resources and produces the twin cohorts needed for approved research projects. The MATR anticipates a greater emphasis on juvenile twins, due to interests of researchers and to the lower costs associated with locating the families of juvenile twins. Because of the MATR's position in the Virginia Institute for Psychiatric

Table 6

MATR Participant Inquiry Topics and Access Method, September–December 2001

Type	N*	%*
Inquiry topics		
Registration related	46	23.1
Returning interviewer call	35	17.6
Address update	34	17.1
Specific study	25	12.6
Wrong person/death	24	12.1
Expertise requested	15	7.5
Miscellaneous	14	7.0
More information	6	3.0
Total	199	100.0
Access method		
Toll-free number	118	59.3
Email	39	19.6
Other telephone	21	10.6
Mail	15	7.5
Total	199	100.0

Note: *Does not include calls resulting from MATR interviewer activities

and Behavioral Genetics, the focus of most future research will continue to be in behavioral and psychiatric topics such as depression, anxiety, conduct disorder, and substance use and abuse. However, individual research projects will change to accommodate new techniques such as molecular genetics (gene-finding projects), affective neuroscience, and structural and functional MRIs to link behavior and health outcomes with brain activity.

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