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Editorial

Twin Family Registries Worldwide: An Important Resource for Scientific Research

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Abstract

Much progress has been made in twin research since our last special issue on twin registries (Hur, Y.-M., & Craig, J. M. (2013). Twin Research and Human Genetics, 16, 1–12.). This special issue provides an update on the state of twin family registries around the world. This issue includes 61 papers on twin family registries from 25 countries, of which 3 describe consortia based on collaborations of several twin family registries. The articles included in this issue discuss the establishment and maintenance of twin registries, recruitment strategies, methods of zygosity assessment, research aims and major findings from twin family cohorts, as well as other important topics related to twin studies. The papers amount to approximately 1.3 million monozygotic, dizygotic twins and higher order multiples and their family members who participate in twin studies around the world. Nine new twin family registries have been established across the world since our last issue, which demonstrates that twin registers are increasingly important in studies of the determinants and correlates of complex traits from disease susceptibility to healthy development.

Keywords: twin family registry; recruitment of twins; zygosity assessment; multiple birth; genetics; environment

The Value of Twin Studies

Throughout the centuries, twins have captured the attention of those around them. While the number of twins born in ancient societies may have been limited due to pregnancy and birth complications, twins were clearly noted as special. Across many different cultures, twins have played a part in mythology and religion. Think, for instance, of Romulus, who is said to have founded Rome, and his twin brother Remus, and of the Biblical story of Esau and Jacob, the twin sons of Isaac and Rachel. The occurrence of twin births in the population made scientists and physicians in ancient times, like today, want to understand the origin of twin similarities and dissimilarities, especially in those cases when the twin individuals were alike in looks. Many different opinions have emerged regarding the causes of twin differences, as is nicely illustrated in the preserved work of Cicero (106 BC–43 BC), the great Roman statesman and philosopher. Cicero notes that the famous physician Hippocrates sought the cause for differences in health between twin individuals in lifestyle differences. The scientist and philosopher Posidonius, however, argued that birth order may have resulted in differences in the constellation of the stars at their time of birth, thereby causing differences in health. It was not till the beginning of the 20th century that it became clear how twins may help us gain insight into causes of individual differences in health and behavior.

Darwin's work on evolution in the mid-19th century and the rediscovery at the start of the 20th century of the work of Mendel, the monk who so painstakingly documented his experiments crossing pea plants, opened the way for the modern-day understanding of genetics. However, it was Sir Francis Galton (1875) who first introduced the concepts of the twin methodology in 1875, followed in 1888 by a paper in which he applied these concepts to anthropometric data (Galton, 1988). Although he did not understand that there was a biological difference between monozygotic (MZ) and dizygotic (DZ) twins, Galton's work provided the impetus to today's use of twin studies to gain insight into the heritability of traits. It took till 1925 before the difference between MZ and DZ twins was firmly established (Lauterbach, 1925), but the first true twin studies were already being conducted

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at that time. One of these studies estimated the heritability of intelligence by comparing the similarity in IQ for MZ and DZ twins (Merriman, 1925).

The first twin registry in the world, The Danish Twin Registry, was established in 1954. Others soon emerged, initially in European countries, but gradually they have spread around the world. The first registers focused on twin pairs, but many now also actively recruit additional family members. Such twin registers have thus become twin family registers, sometimes including several generations consisting of twins, their siblings, spouses, children, parents and even grandparents. The inclusion of these different types of family members does not only increase power but also allows for a test of additional hypotheses regarding cultural *versus* genetic transmission and assortative mating, as well as testing the generalizability of the findings in twins as compared to non-twin or singleton populations.

In addition to expanding from twins to twin families, registries have also grown in the amount of information available on individuals enrolled, especially since most registers follow their participants longitudinally. Moreover, a wide variety of instruments are used to obtain information. Participants complete surveys on a large range of traits and may undergo a wide range of tests, such as cognitive tests, MRI scans and psychophysiological and cardiovascular assessments. In addition, they provide biological samples such as tissue, hair, blood, saliva and feces, which allow for the measurement of hormones, metabolites, proteins and gut microbiome. At times, additional sources of information on twins, such as teachers or physicians, may also be approached, and information may also be added *via* linkage to external databases, such as national cancer registers. This has resulted in a large number of heritability studies covering almost any phenotype you can imagine, as well as significant success in genomewide association, epigenomewide association and other omics studies in recent years. For an extensive overview of heritability studies, see, for example, Polderman et al. (2015).

It has been argued that twin studies, given the current large national biobanking efforts ongoing in a number of countries, are at risk of becoming obsolete. Nothing is further from the truth! This is well illustrated in van Dongen et al's (2012) article on the value of twins in the 'omics' era. While the focus of twin studies may have been on establishing the heritability of a wide variety of phenotypes, twin studies still offer many other unique ways to gain insight into the mechanisms that drive individual differences. This includes but is not limited to the discordant MZ design, which provides the ultimate case-control matching for genetic profile, pregnancy, age, sex and childhood environment. Not only for phenotypic information do these studies remain informative, but they may also shed light upon the effects of (epi)genetic alterations occurring right after conception or across the lifespan, such as *de novo* mutations, DNA methylation and RNA expression. Recent twin studies, including both MZ and DZ twins have shown that many of these genetic adaptations to environments may also be genetically driven and the extensive collection of data, both phenotypically and genetically, allows for a thorough examination of the gene–environment interplay in human development and health. Therefore, it is not surprising that the established twin registries continue to make significant contributions to our understanding of the causes of individual differences and that new twin registeries are still being created.

Table 1. Highlights of twin family registries established since our last special issue (Hur & Craig, 2013)

Study logo (or national flag)	A brief description of the registry
The University of Sao Paulo Twin Panel (2017)	• To study genetic and environmental influences on psychological traits in Brazilians • Twins recruited from the University of Sao Paulo and by media
Mexico Twin Registry (MexTR) (2019)	• To study genetic basis of health and related behaviors in the Mexican population • Twins recruited from public records of all university students in the State of Jalisco, Mexico for the past 20 years
Mexican Twin Registry (2018)	• To perform epidemiological and genetic research on health and diseases in the Mexican population • Twins recruited by social media, public campaigns
Children of TEDS (CoTEDS; 2016)	• To investigate intergenerational associations on mental health and cognitive traits across child developmental stages • Participants recruited from children of the Twins Early Development Study (TEDS) in England
Twinlife (2019)	• To study prenatal influences on neurodevelopmental impairment and diseases using monochorionic (MC) twins • MC twins recruited from hospitals in the Netherlands
Serbian Twin Registry (2014)	• To perform behavior genetic studies of psychological traits in Serbians • Twins recruited by public campaigns, media, twin festivals
Avera Twin Register (2016)	• To study environmental and genetic influences on health, illness prevention, behavior and diseases • Twins recruited from Midwestern states in the USA by media campaigns
National Project on Achievement in Twins (2017)	• To study co-development of reading and math performance • Twins recruited from elementary schools in all US states
Isfahan Twin Registry (2017)	• To study epigenetic and genetic causes of diseases, especially cancer, diabetes and cardiovascular diseases • Twins recruited from welfare agencies, maternity hospitals, etc. in Isfahan, Iran

New Twin Family Registries

Table 1 lists new twin family registries established since our last special issue (Hur & Craig, 2013). Note that a number of these new registries are located in South America, a continent that until recently has seen little twin research (see also Figure 1). In Brazil,

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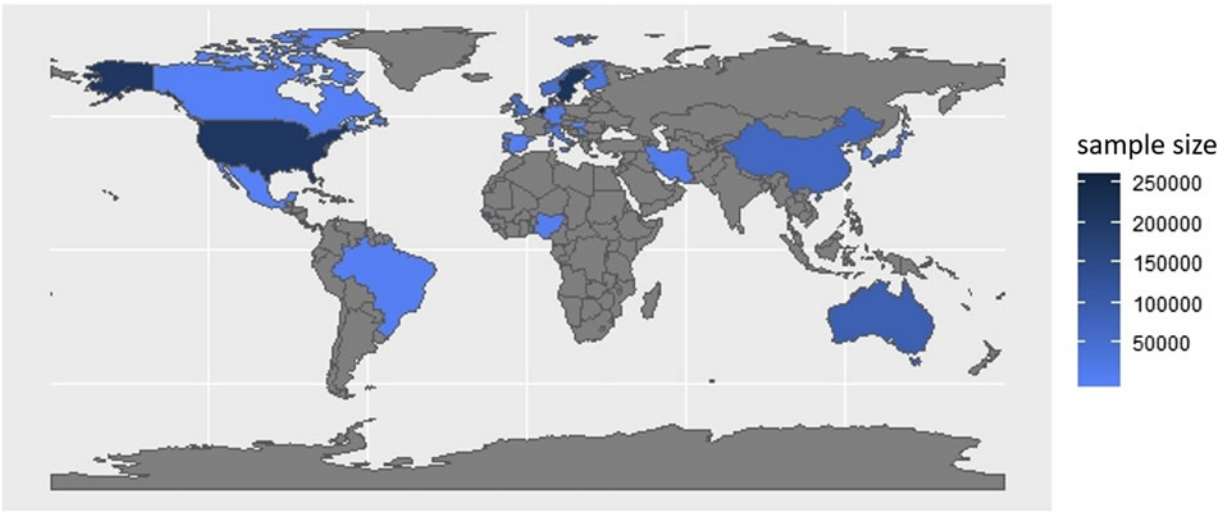

Fig. 1. Location of twin studies featured in this issue.

the University of Sao Paulo Twin Panel (the USP Twin Panel) recruits twins from the University of São Paulo and other regions using social media campaigns and through annual festivals offering recreational and cultural activities to twins and their families. In Mexico, two twin family registries have emerged to study genetic underpinnings of health and related behaviors in the Mexican population. The first one, the Mexico Twin Registry (MexTR), attempts to identify twins from public records of all university students in the state of Jalisco in Mexico for the past 20 years by matching birth date and family name. In addition, they recruit young twins from the largest maternity hospital in the state and a multiple birth association in Mexico. The second one, the Mexican Twin Registry (TwinsMX), was established by a multidisciplinary research team at the Universidad Nacional Autónoma de México in collaboration with Australian twin researchers. They have established an electronic questionnaire portal and recruit twins and multiples of all ages living in five highly populated states in Mexico using social media, advertising and publicity campaigns.

While Europe already has a large number of established twin registries, new ones still arise. Sometimes they emerge from another twin registry, like the Children of the Twins Early Development Study (CoTEDS), which constitutes the children of adult twins who have participated in the Twins Early Development Study (TEDS) since infancy. As the TEDS investigated parents of their twins as well, it is now possible for the CoTEDS to utilize three-generation pedigrees. These extensive pedigree data make it possible to disentangle passive gene–environment correlations from the associations between parental characteristics and children's outcomes, as well as estimate the role of genetic factors in explaining intergenerational associations (McAdams et al., 2018).

A unique stand-alone study in the Netherlands may help advance our understanding of the role of intrauterine environment in human development and diseases in singletons as well as in twins. The Twin Longitudinal Investigation of Fetal discordance (Twinlife) in the Netherlands is a newly developed unique resource comprised of monochorionic (MC) twins. As MZ twins, the MC twins share genetic make-up as well as many environmental factors. However, they are also frequently exposed to vastly different prenatal environments due to complications associated with sharing a single placenta. MC twins in Twinlife are assessed at 14 weeks of gestation and will be followed until they reach 8–9 years of age.

The Serbian Twin Registry (STR) is the first large-scale, national twin family registry in Serbia. They recruit twins and their family members through public campaigns, media and twin festivals. Since 2014, the investigators of the STR, comprised of a multidisciplinary team, have collected phenotypic and molecular genetic data on psychological characteristics and mental health in Serbians. Preliminary findings are described in this issue.

Two new twin registries have also emerged in the USA. The Avera Twin Register (ATR) has recruited twins of all ages in South and North Dakota, Iowa, Nebraska and Minnesota since 2016. In close partnership with the Netherlands Twin Register (NTR), the ATR aims to study environmental and genetic influences on health and diseases longitudinally with a repository of genetic materials of twins and their family members. The National Project on Achievement in Twins (NatPAT) aims to recruit approximately 3000 volunteer twin pairs attending elementary schools in all states in the USA. By linking twins in the NatPAT to the DIBELS Data System (DDS), an online repository that contains student performance on reading and math assessments for approximately 1.4 million children in the USA, the NatPAT seeks to discover salient factors that contribute to the co-development of reading and math performance during the critical developmental period of elementary school.

An Overview of Twin Family Registries in the World

In total, 61 papers from 25 countries, including three international consortia, were compiled in this issue (Figure 1, Table 2). The papers amount to approximately 1.3 million MZ, DZ twins and higher order multiples and their family members who participate in twin studies around the world, serving as a resource for thousands of scientific publications across a wide range of disciplines including psychology, education, sociology, sports science, medicine, pharmacology and epidemiology.

Statistical power calculations have shown that large sample sizes are critical to resolve sources of familial resemblance in quantitative and molecular genetic twin studies (Martin et al., 1978; Posthuma & Boomsma, 2000; Verhulst, 2017). As shown in Table 2, the sample sizes of registries across the world vary

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Table 2. An overview of twin family registries worldwide

Country	Name of the registry	Target region	Major recruitment methods	Total sample size	Subjects	Age in years	ZYG	Major phenotypes	DNA (bio-sample collection)?	Email	Website
Australia	Twins Research Australia	National	Twin pregnancy booklet, internet, media, Facebook, MBA	45,000 pairs	MZ, DZ, OSDZ	All ages	Q+ DNA	Health, psychological traits	Yes	John Hopper; j.hopper@unimelb.edu.au	www.twins.org.au
	Peri/Postnatal Epigenetic Twin Study (PETS)	Melbourne	Mothers recruited in pregnancy	250 pairs	MZ, DZ, OSDZ and their parents	10–12	DNA	Cardiometabolic, neurodevelopmental	Yes	Jeffrey Craig; jeffrey.craig@deakin.edu.au	https://www.mcri.eduau/peripostnatal-epigenetic-twins-study-pets
Belgium	The East Flanders Prospective Twin Survey	East Flanders	Birth records	20070	MZ, DZ, OSDZ and triplets	0–46	DNA, chor	Pre/perinatal influences on behavior and diseases	Yes	Catherine Derom; c.derom@telnet.be	www.twins.be
	TwinssCan	East Flanders	East Flanders Prospective Twin Survey	1202	MZ, DZ, OSDZ and their families	15–35	Q+ DNA	Psychopathology	Yes	Bart Rutten; b.rutten@maastrichtuniversity.nl	
Brazil	University of Sao Paulo Twin Panel	National	University of Sao Paulo, media	4826	MZ, DZ, OSDZ, triplets+	All ages	Q+ DNA	Psychological traits, anthropometric variables	Yes	Emma Otta; emmaotta@usp.br	https://www.paineluspdegemeos.com.br/
Canada	Quebec Newborn Twin Study	Quebec	Birth records	1324	MZ, DZ, OSDZ	0–19	DNA	Cognitive, behavioral and social-emotional components of developmental health	Yes	Michel Boivin; michel.boivin@psy.ulaval.ca	
China	Chinese National Twin Registry	National	Center for Disease Control, media	61,566	MZ, DZ, OSDZ, triplets+	All ages	Q+ DNA	Diseases, public health variables	Yes	Liming Li; lmlee@vip.163.com	
	Beijing Twin Study	Beijing	Public schools	1387 pairs	MZ, DZ, OSDZ, triplets+	10–18	Q+ DNA	Psychopathology, psychological traits	Yes	Xinying Li; lixy@psych.ac.cn	
	Guangzhou Twin Eye Study	Guangzhou	Guangzhou City Bureau of Statistics	1300 pairs	MZ, DZ, OSDZ, triplets+	7–30	DNA	Ocular data, anthropometry, cardiovascular risk factors	Yes	Mingguang He; mingguang_he@yahoo.com	
Denmark	Danish Twin Registry	National	Church records, Danish civil registration system, Conscription register, MBA	175,518	MZ, DZ, OSDZ, triplets+ and their families	10 to 100+	Q+ DNA	Diseases, lifestyle/health-related behaviors, aging, cognitive and physical abilities, depression symptomatology, socioeconomic status	Yes	Kaare Christensen; kchristensen@health.sdu.dk	https://www.sdu.dk/en/Om_SDU/Institutter_centre/Ist_sundhedstjenesteforsk/Centre/DTR.aspx
England	Twins Early Development Study	National	Birth records	16,000 pairs	MZ, DZ, OSDZ	2–21	Q+ DNA	Cognitive, emotional and behavioral development	Yes	Robert Plomin; robert.plomin@kcl.ac.uk	https://www.teds.ac.uk
	Children of the Twins Early Development Study	National	TEDS	554	Children of TEDS	0–11	Q+ DNA	Child psychopathology, temperament, cognitive development	No	Tom McAdams; tom.mcadams@kcl.ac.uk	https://www.teds.ac.uk/co-teds
	TwinsUK	National	Media campaign	14,686	MZ, DZ, OSDZ	18–82	Q+ DNA	Complex diseases and aging	Yes	Tim Spector; tim.spector@kcl.ac.uk	http://twinsuk.ac.uk/

Finland[a]	FinnTwin16	National	Central Population Register of Finland	30,527	MZ, DZ, OSDZ, triplets+ and their siblings, parents	16–35	Q+ DNA	Substance use/ dependence, lifestyle, mental and somatic health, psychosocial and socioeconomic traits	Yes	Jaakko Kaprio; jaakko.kaprio@helsinki.fi	www.twinstudy.helsinki.fi
Germany	German Twin Family Panel	National	Community registration office	4097 pairs and families	MZ, SSDZ and their siblings, parents, partners	5–25	Q+ DNA	Social inequalities	Yes	Bastian Moenkediek; bastian.moenkediek@uni-bielefeld.de	https://www.twin-life.de/en
	Study of Personality Architecture and Dynamics	National	Media, twin clubs, city registration offices	1962	MZ,DZ, OSDZ, triplets+ and their spouses, children, parents	14–94	Q	Personality and related traits	No	Christian Kandler; ckandler@uni-bremen.de	www.speady.de/studies/?lang=en
Guinea-Bissau	Guinea-Bissau Twin Registry	Center and six suburban areas of Bissau	Hospital, population-based	3600	MZ, DZ, OSDZ and singleton controls	0 to young adults	Q+ DNA	Metabolic disease, childhood twin mortality	Yes	Morten Bjerregaard-Andersen; mban@dadlnet.dk	
Hungary	Hungarian Twin Registry	National	Media, previous databases, twin registries, from 2019: national database	1044 pairs	MZ, DZ, OSDZ and their families	All ages	Q	Health-related variables and diseases (e.g., radiogenomics, musculoskeletal, cardiovascular and respiratory diseases), psychology, sociology	Yes	Adam Domonkos Tarnoki; tarnoki2@gmail.com	www.ikrek.hu
Israel	Longitudinal Israeli Study of Twins	National	The Ministry of Interior	1657 families	MZ, DZ, OSDZ and their parents	3–15	Q+ DNA	Prosocial behavior, empathy, temperament, values, parenting	Yes	Ariel Knafo-Noam; ariel.knafo@huji.ac.il	https://soclabweb.wixsite.com/home/home
Italy	Italian Twin Registry	National	Municipality registry offices, maternity hospitals	29,000	MZ, DZ, OSDZ and their families	0–95	Q+ DNA	Mental health, psychological traits, health-related variables	Yes	Stazi Maria Antonietta; antonia.stazi@iss.it	https://scic.iss.it/gemelli/
Iran	Isfahan Twins Registry	National	Welfare agencies, public health homes, public and private nursing homes	1000	MZ, DZ, OSDZ, triplets+	All ages	Q+ DNA, Nail, hair	Health and lifestyle related variables, behaviors and disease	Yes	Mojgan Gharipour; mojgangharipour@gmail.com, Nizal Sarrafzadegan; nsarrafzadegan@gmail.com	

(*Continued*)

Table 2. (*Continued*)

Country	Name of the registry	Target region	Major recruitment methods	Total sample size	Subjects	Age in years	ZYG	Major phenotypes	DNA (bio-sample collection)?	Email	Website
Japan	Twin Database of the Secondary School Attached to the University of Tokyo	National	Schools	About 1400	MZ, DZ, OSDZ and their families	11–85	Q+ DNA	Physical growth, allergy, lifestyle, metabolic diseases	Yes	Toshimi Ooma; tooma@ad.wakwak.com	
	Japanese Database of Families with Twins and Multiples	National	Twins mothers clubs	563 pairs	MZ, DZ, OSDZ and their families	0–6	Q	Physical growth, health	No	Toshimi Ooma; tooma@ad.wakwak.com	
	Keio Twin Research Center	National	Government resident register	10,691 pairs	MZ, DZ, OSDZ	3–52	Q+ DNA	Psychological traits, education related variables, mental health	Yes	Juko Ando; juko@msa.biglobe.ne.jp	
	Osaka University Center for Twin Research	National	Media, posters	3000	MZ, DZ, OSDZ	All ages	DNA	Physical growth, health, dental phenotype	Yes	Norio Sakai; norio@sahs.med.osaka-u.ac.jp	
	West Japan Twins and Higher Order Multiple Births Registry	National	MBA, public health centers	12,041	MZ, DZ, OSDZ, triplets+	0–40	Q	Maternal and child health of families with multiples; physical growth	No	Yoshie Yokoyama; yyokoyama@nurs.osaka-cu.ac.jp	
Korea, Republic	South Korean Twin Registry	National	Schools, maternity hospitals, MBA	4058	MZ, DZ, OSDZ	1–30	Q	Psychological traits, mental health	No	Yoon-Mi Hur; ymhur@mokpo.ac.kr	
Mexico	Mexico Twin Registry (MexTR)	State of Jalisco	Public records of university students, MBA, maternity hospital	Under plan	MZ, DZ, OSDZ	All ages	NA		Under plan	Guillermo A. Cervantes-Cardona; gacervantes66@hotmail.com	
	Mexican Twin Registry (TwinsMX)	National	social media, public campaigns	145	MZ, DZ, OSDZ	18–60	Q	Somatic and mental health psychometrics, lifestyle	Yes	Alejandra Medina-Rivera; amedina@liigh.unam.mx, Miguel E Renteria; miguel.renteria@qimrberghofer.edu.au	https://twinsmxofficial.unam.mx/
The Netherlands	Twin Longitudinal Investigation of Fetal Discordance	National	Hospital	Plan to have 100 pairs+	Monochorionic twin pairs	Prenatal to 8	Chor	(Fetal) growth, cardiovascular diseases, neurodevelopmental impairment	Yes	B. T. Heijmans; b.t.heijmans@lumc.nl	www.twinlifestudy.info
	The Netherlands Twin Register	National	City councils; commercial birth felicitation service; Dutch society of parents of multiples	255,785	MZ, DZ, OSDZ and their families	All ages	Q+ DNA	Psychological variables, mental health, physical growth	Yes	Dorret Boomsma; di.boomsma@vu.nl	http://www.tweelingenregister.org/

Nigeria	Nigerian Twin and Sibling Registry	Lagos State, Abuja, FTC	Schools	5323	MZ, DZ, OSDZ, triplets and singletons	10–21	DNA	Psychological traits, mental health	Yes	Yoon-Mi Hur; ymhur@mokpo.ac.kr	
Norway	Oslo University Adolescent and Young Adult Twin Project	National	Birth records	4668 twin pairs and families	MZ, DZ, OSDZ and their families	12–22	Q+ DNA	Psychological variables (personality), mental health	No	Sven Torgersen; svenn.torgersen@psykologi.uio.no, Trine Waaktaar; trine.waaktaar@psykologi.uio.no	
	Norwegian Twin Registry	National	Birth records, record linkages of national registries	32,664	MZ, DZ, OSDZ	28 and older	Q+ DNA	Somatic and mental health	Yes	tvilling@fhi.no	
Portugal	Portuguese Healthy Family Study	National	Public schools	12,385	Singleton children and their parents, sibling pairs	All ages	NA	Physical activity, body composition and physique, fitness and metabolic syndrome	Mo	Jose Maia; jmaia@fade.up.pt	
Serbia	Serbian Twin Registry	National	Public campaigns, media, twin festival	1658	MZ, DZ, OSDZ and their family members	All ages	Q+ DNA	Psychological characteristics, anthropometric measures, mental and somatic health	Yes	Snezana Smederevac; snezana.smederevac@uns.ac.rs	http://www.blizanci.rs
Spain	Murcia Twin Registry	Murcia	University, birth records	3545	MZ, DZ, OSDZ, triplets+	20+	Q+ DNA	Health-related variables	Yes	Juan Ordonana; ordonana@um.es	https://www.um.es/registrogemelos/
Sweden	Swedish Twin Registry	National	Birth records	216,258	MZ, DZ, OSDZ	All ages	Q+ DNA	Mental and somatic diseases, behavior	Yes	Patrik Magnusson; patrik.magnusson@ki.se	http://ki.se/en/research/the-swedish-twin-registry
USA	Arizona Twin Project	Arizona	Birth records	700	MZ, DZ, OSDZ	1–11	Q+ DNA	Developmental psychopathology and somatic health	Yes	Kathryn Lemery-Chalfant; klemery@asu.edu	
	Avera Twin Register	National	Media campaign	838	MZ, DZ, triplets+, siblings and their parents	All ages	Q+ DNA	Lifestyle, aging, diseases	Yes	Julie Kittelsrud; Julie.Kittelsrud@Avera.org	www.avera.org/twin-register
	Boston University Twin Project	Massachusetts	Birth records	310 pairs	MZ, same-sex DZ	Birth to age 5	DNA	Temperament and related behaviors	Yes	Kimberly Saudino; ksaudino@bu.edu	
	CATSLife	Colorado	Adoption agencies	776	Adoptees and their birth and adoptive parents	0–40	NA	Behavioral development, cognitive aging, health	Yes	Sally Wadsworth and Chandra Reynolds; sally.wadsworth@colorado.edu, chandra.reynolds@ucr.edu	
	Colorado Twin Registry	Colorado	Schools, birth records	4500	MZ, DZ, OSDZ and their families	0–40	Q+ DNA	Psychological traits (cognitive abilities, substance use and abuse, health, etc.)	Yes	Robin Corley; robin.corley@colorado.edu	https://www.colorado.edu/ibg/research/human-research-studies/colorado-twin-registry
	Early Growth and Development Study	National	Adoption agencies	2456	Adoptees and their birth and adoptive parents and siblings	0–20	NA	Temperament, behavior problems, mental health, obesity, achievement	Yes	Leslie Leve; leve@uoregon.edu	https://www.egdstudy.org/

(*Continued*)

Table 2. (*Continued*)

Country	Name of the registry	Target region	Major recruitment methods	Total sample size	Subjects	Age in years	ZYG	Major phenotypes	DNA (bio-sample collection)?	Email	Website
	Florida State Twin Registry	Florida	Schools	5593	MZ, DZ, OSDZ, triplets+	11–22	Q	Reading development, school achievement, behaviors	No	Jeanette Taylor; taylor@psy.fsu.edu	
	Fullerton Virtual Twin Project	National	Media, multiple birth organizations, personal referrals	169	Virtual twins	4.01–54.84	NA	Psychological traits	No	Nancy Segal; nsegal@fullerton.edu	
	Louisville Twin Study	Kentucky	LTS database	1770	MZ, DZ, triplets+, siblings, children of twins	All ages	Q+ DNA	Psychological, physical growth	Yes	Deborah Davis Winders <deborah.davis@louisville.edu> or twins@louisville.edu	
	Michigan State University Twin Registry	Michigan	Birth records, university	30,000	MZ, DZ	3–55	Q+ DNA	Internalizing and externalizing psychopathology	Yes	S. Alexandra Burt and Kelly Klump; burts@msu.edu and klump@msu.edu	https://msutwinstudies.com/
	Minnesota Center for Twin and Family Research	Minnesota	Birth records	23,199	MZ, DZ, adoptees	7 to old adults	Q+ DNA	Substance use and related psychopathology	Yes	Rachel Hawley; mctfr@umn.edu; 1-800-462-8946	https://mctfr.psych.umn.edu/
	Mid-Atlantic Twin Registry of Virginia Commonwealth University	Virginia, North and South Carolina	Birth records, schools	54,042	MZ, DZ, triplets+ and their families	All ages	Q+ DNA	Developmental psychopathology	Yes	Emily Lilley; matr@vcu.edu	www.matr.vcu.edu
	NAS-NRC Twin Registry and Duke Twin Study of Memory in Aging	National	Birth records linked with army records	31,848	Male MZ and DZ	15–82	Q+ DNA	Anthropometric, health and mortality, education and earnings	Yes	Margaret Gatz; gatz@usc.edu	
	National Project on Achievement in Twins	National	Schools	2514	MZ, DZ, OSDZ	4.25–14.25	Q	Reading development, school achievement, behaviors	No	Sara Hart; hart@psy.fsu.edu	http://www.idcdlab.com/natpat-twin-project.html
	Pennsylvania Longitudinal Study of Parents and Children	Pennsylvania	Schools, birth records	2260	MZ, DZ, OSDZ, triplets+ and their parents	0–88	Q	Mental and somatic health, prosocial traits	No	Jenae Neiderhiser; jenaemn@gmail.com	
	Project Talent Twin and Sibling Study	National	Schools	5003	MZ, DZ, OSDZ, triplets+ and their siblings	14–78	Q and photo	Cognition, personality, education, occupation, activities, health, aging	No	Carol Prescott; cprescot@usc.edu	projecttalent.org
	Southern Illinois Twins/Triplets and Siblings Study	Illinois	Media, birth records	1175	MZ, DZ, OSDZ, triplets+, siblings	1–20	Q+ DNA	Childhood aggression, parent–child interaction, emotional development	Yes	Lisabeth DiLalla; Ldilalla@siu.edu	https://www.siumed.edu/playlab/twin-play-lab.html; https://www.facebook.com/SITSS.SIU

	Vietnam Era Twin Study of Aging	National	Army records	1230	Male MZ, DZ	50–70	DNA	Cognitive and brain aging, Alzheimer's disease	Yes	William Kremen; wkremen@ucsd.edu	
	Washington State Twin Registry	Washington State	Department of Licensing	9668 pairs	MZ, DZ, OSDZ	All ages	Q+ DNA	A variety of somatic and mental health outcomes	Yes	Glen Duncan; glen.duncan@wsu.edu	https://wstwinregistry.org/
	Wisconsin Twin Project	Wisconsin	Birth records	5000 pairs	MZ, DZ, OSDZ	Prenatal to 24	Q+ DNA	Temperament, affective neuroscience, developmental psychopathology, puberty	Yes	Hill Goldsmith; hill.goldsmith@wisc.edu	https://goldsmithtwins.waisman.wisc.edu/
Consortia	Collaborative Project of Development of Anthropometrical Measures in Twins (CODATwins)	24 countries	Twin registries in the participating countries	489,981	MZ, DZ, OSDZ	o to about 90	Q+ DNA	Height, BMI, education, smoking		Karri Silventoinen; karri.silventoinen@helsinki.fi	
	Interplay of Genes and Environment across Multiple Studies (IGEMS)	Australia, Denmark, Finland, Sweden and USA	Twin registries in the participating countries	76,233	MZ, DZ, OSDZ	14–103	Q+ DNA	Dementia, mortality, physical, SES and psychological functioning		Nancy Pedersen; nancy.pedersen@ki.se	https://dornsife.usc.edu/labs/igems/
	Nordic Twin Study on Cancer (NorTwinCan)	Denmark, Finland, Norway and Sweden	Twin registries in the participating countries	315,413	MZ, DZ, OSDZ		Q+ DNA	Cancer		Jennifer Harris; Jennifer.Harris@fhi.no	

Note: Numbers in 'Total sample size' refer to individual twins unless 'pairs' are stated. ZYG = zygosity assessment methods; MZ = monozygotic twins, DZ = dizygotic twins; OSDZ = opposite-sex dizygotic twins; SSDZ = same-sex dizygotic twins; MBA = multiple birth association; Chor = chorionicity. Q = questionnaire method, NA = not applicable; Q+ DNA = questionnaire supplemented by DNA testing.

[a] Finland has two other twin family registries: see Rose et al. (2019) for the FinnTwin12 cohort and Kaprio et al. (2019) for the Older Finnish Twin Cohort.

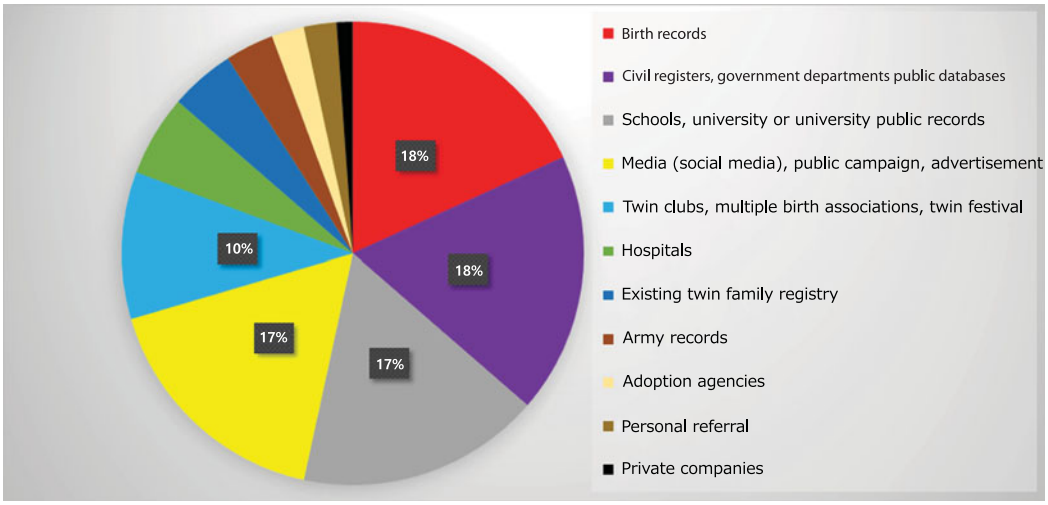

Fig. 2. Frequencies of major recruitment methods used by twin family registries included in the current special issue.

considerably from less than 200 to nearly 200,000 (The Danish Twin Registry) or over 200,000 (The NTR, The Swedish Twin Registry), with approximately 39% of the registries having more than 10,000 participants. The total number of participants differs greatly by continent. Europe has the largest number of participants (over 870,000), while Latin America has the smallest ($N \approx 5000$). Although most twin family registries collect opposite-sex as well as same-sex twins, a few registries collect only same-sex twins. Data on opposite-sex twins enable us to address many research issues, including but not limited to the effects of prenatal hormone transfer and sex differences in genetic and environmental contributions to behaviors and diseases.

Many twin researchers seek to recruit twins of all ages, but others look at specific age groups. The vast majority of the twin family registries are national, encompassing 19 countries. However, twin researchers in the USA tend to develop state-specific twin family registries. Currently, there are 11 statewide twin family registries in the USA in addition to several nationwide ones. While most twin family registries were established in affluent Western nations, some registries were founded in developing countries, offering valuable opportunities to evaluate the influence of worldwide environmental variations as well as to strengthen studies of genotype–environment interaction (G × E) across the world.

Figure 2 shows recruitment methods used by twin family registries covered in the current special issue. Most registries identify twins through birth records, government departments and various civil registers. However, schools, media advertisements, social media and public campaigns are also very frequently employed to recruit twins. Additionally, many twin registries are associated with twin clubs, multiple birth associations, maternity hospitals in the country and annual twin festivals to recruit twins. A few twin registries use existing twin registries to identify twins (e.g., TwinssCan from EFPTS, CoTEDS from TEDS, the Louisville Twin Study from the old LTS database). As each method has strengths and weaknesses, and legislation related to access to the public records differ by country, many twin registries tend to utilize several of these recruitment methods simultaneously to maximize their sample sizes and the representativeness of the sample.

Twin family registries use a number of strategies to maintain twins' interests in active participation in research. Such strategies include giving twins and their parents' feedback on psychological and health assessments, gift coupons and monetary compensation. Holding annual festivals and other social events, and sending birthday cards and regular newsletters containing twin research findings to twins and their families are other frequently used strategies.

Investigators of twin family registries in this issue have collected a wide range of phenotypes and environmental data from twins and their family members. Most frequently collected phenotypes include anthropometry variables encompassing physical growth, socioeconomic traits, psychological traits including cognitive abilities and personality, home/school environment, and physical and mental health variables and related behaviors (e.g., lifestyle). However, some registries are specialized in more or less specific phenotypes such as ocular traits (The Guangzhou Twin Eye Study), dentition (The Osaka University Center for Twin Research) or the impact of fetal discordance in MC twins (the Twin Longitudinal Investigation of Fetal Discordance).

Twins' zygosity is often incorrectly labeled by delivering physicians. However, accurate information about zygosity is important to twin researchers as well as to twins and their parents. Odintsova et al. (2018) have shown that misclassification of zygosity of twins can lower heritability estimate up to 20% depending on the phenotype. Additionally, it has been found that knowledge of true zygosity status provides twins and their parents' peace of mind and positive emotional responses (Cutler et al., 2015). Although zygosity can be determined using the standard questionnaire method, DNA testing using sufficient markers is the most accurate method of zygosity assessment. Over 80% of twin registries in this issue confirmed that their zygosity assessment was done on the basis of DNA testing alone or a questionnaire method complemented by DNA testing, suggesting that overall the reliability of zygosity assessment in twin studies is quite high. With the reduction in genotyping costs and the increasing interest in genome-wide association studies among twin researchers, the DNA method of zygosity assessment will be increasingly used in the future.

Data collection methods vary greatly by phenotype, research interests and availability of funding. Mail and telephone surveys, laboratory assessments and face-to-face interviews have been used

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traditionally by many twin researchers in different fields. More recently, however, web- and mobile-based assessment methods are becoming increasingly popular because these methods enable the collection of large amounts of data with relatively little time and cost. Also, record linkages of twin family registers to national health, education and administrative registers are carried out widely, especially in many European countries, to create large-scale, high-quality and nationally representative datasets without selection bias.

Consortia Using Twin Family Registries

Collaborations across twin registries provide a richer database to test various hypotheses. Three articles in this issue describe international consortia based on twin family registries: Collaborative Project of Development of Anthropometrical Measures in Twins (CODATwins), the Consortium on Interplay of Genes and Environment across Multiple Studies (IGEMS) and the Nordic Twin Study on Cancer (NorTwinCan). The CODATwin consortium is based on anthropometry measures and related data collected from twin family registries in 24 countries (total $N = 489{,}981$ twins). Its main goal is to determine factors that modify genetic and environmental variations of body size measures across populations. IGEMS was established to explore the nature of gene–environment interplay in physical and psychological functioning, dementia and mortality across adulthood. It includes data from 76,233 twins coming from 18 twin family registries from 5 countries: Sweden, Denmark, Finland, the USA and Australia. NorTwinCan was constructed by linking twin family registries of Denmark, Finland, Norway and Sweden to their country-specific national cancer and cause-of-death registries (total $N = 315{,}413$ twins) to understand familial effects on cancer incidence and mortality, and cross-cancer associations. The articles in this issue provide a description of the consortia, their major findings to date, current research highlights and future research directions.

Conclusions

This special issue provides a comprehensive, but not exhaustive, overview of twin family registries around the world. The number of twin family registries will likely increase and expand with greater availability of databases covering various human populations in the future. It is now well recognized that large, population-based twin family registries worldwide have substantially improved our knowledge of important factors underlying population variabilities in common, complex traits and diseases. Overall, twins are representative of the general population. Twin research remains of value and may be used to further explore findings in the general population. Twin registries have kept pace with the technological developments and now include many different types of data applying the latest statistical techniques. As such, the contribution of twin family registries to formulating new research strategies is high and the viability of twin studies is ensured for the future. Twin births occur across all strata of the population, and due to the widespread use of artificial reproductive technologies the number of twins has increased sharply across the world. In addition, twins and their family members are often enthusiastic participants in twin study projects.

Investigators in twin family registries welcome collaborations to exchange insights, knowledge and database that will lead to benefits in science and human societies. We encourage researchers interested in collaboration and access to the data to contact the investigators of the relevant registry (see contact information in Table 2). We hope you enjoy reading about twin family registries in this special issue and we are looking forward to many new partnerships!

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