

Australian Twin Registry: A Nationally Funded Resource for Medical and Scientific Research, Incorporating **match** and WATCH

John L. Hopper,¹ Susan A. Treloar,^{1,2} Nicholas H. de Klerk,³ and Ruth Morley⁴

¹ Australian Twin Registry, Centre for Molecular, Environmental, Genetic and Analytic Epidemiology, The University of Melbourne, Australia

² Genetic Epidemiology Laboratory, Queensland Institute of Medical Research, Australia

³ Western Australian Twin Child Health (WATCH) Study, Department of Biostatistics and Genetic Epidemiology, Telethon Institute for Child Health Research and Centre for Child Health Research, The University of Western Australia, Perth, Australia

⁴ Mothers and Twin Children (**match**), Department of Paediatrics and Murdoch Children's Research Institute, The University of Melbourne, Australia

The Australian Twin Registry (ATR) has, since the late 1970s, enrolled more than 30,000 pairs of all zygosity types and ages willing to consider participation in approved research studies. Its core functions are the recruitment to, and maintenance of, an up-to-date database containing contact details and baseline information, and the management of fair and equitable access so as to enhance medical and scientific research. The ATR has facilitated more than 430 studies producing 525 peer-reviewed publications using a variety of designs including classic biometrical twin and twin family studies, co-twin control studies, intervention studies, longitudinal studies, and studies of issues relevant specifically to twins. The ATR is supported for 2004 to 2009 by an Australian National Health and Medical Research Council (NHMRC) Enabling Grant, a new form of funding which recognizes the importance of long-term support for shared national resources. New initiatives include: integration with the Western Australian Twin Child Health (WATCH) cohort and the new Western Australian Twin Registry (WATR); foundation of a cohort of mothers and their twin children recruited from the time of diagnosis of the multiple gestation (**match**); a national Twins Festival run in collaboration with the Australian Multiple Birth Association (AMBA); promotion of the ATR at medical conferences; and fostering an active network of researchers from a range of disciplines and providing financial support for new researchers to attend international twin research workshops. Consistent with its mission statement, the long-term goal of the ATR is to make twin studies a standard component of medical and scientific research.

The Australian Twin Registry (ATR) was established in the late 1970s as a national volunteer registry of Australian twin pairs of all zygosity types and ages. A

brief history of the ATR is recorded in an earlier paper (Hopper, 2002). Twins are eligible to join regardless of their health or medical history. The ATR manages information from more than 30,000 enrolled twin pairs and higher order multiples, and provides researchers with access to twin pairs suitable for specific studies once proposals are approved and twins have agreed to participate. Its core functions are the maintenance of an up-to-date database containing contact details and baseline information for twins willing to consider participating in research projects, and the management of access to that resource in ways that enhance research capacity within Australia in a fair and equitable manner while protecting the rights of twins.

The ATR does not undertake research itself but acts as facilitator, providing an important national and international resource for medical and scientific researchers across a broad range of disciplines. Its broad aim is to enable studies of the impact of genetic and environmental factors on health, and on the treatment and prevention of disease. As an openly shared resource, the ATR provides researchers with access to an established infrastructure and a network of scientists and administrative staff who are experienced in twin research. Current studies utilizing the ATR are run by a wide range of researchers from Australian institutes including the Queensland Institute for Medical Research, Curtin University, The University of Melbourne, and The University of Adelaide. Some studies are conducted in collaboration with overseas researchers from Europe, North

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Address for correspondence: John L. Hopper, Centre for Molecular, Environmental, Genetic and Analytic Epidemiology, The University of Melbourne, Level 2, 723 Swanston Street, Carlton, VIC 3053, Australia. E-mail: j.hopper@unimelb.edu.au

America and elsewhere, including the Netherlands Twin Register and the Finland Twin Register.

Mission

The ATR's mission is to facilitate medical and scientific studies that involve at least in part the participation of twin pairs, and use the special features that arise from twin designs to enable questions about health and well-being to be answered in ways that they otherwise could not. The ATR also uses its influence and resources to support studies of topics of particular relevance to the health and well-being of twins themselves. That is, the underpinning aim of the ATR is to use the special characteristics of twin pairs to make a difference to health and well-being.

Funding

The ATR is supported by an Australian National Health and Medical Research Council (NHMRC) Enabling Grant for the period 2004 to 2009. This new grant scheme responds directly to the recommendations of the Wills Report (see Health and Medical Research Strategic Review [Wills Report]¹) and provides support for specific facilities and/or activities that will enhance the national health and medical research effort across a broad range of disciplines. Enabling Grants are subject to the principles of excellence, an open and competitive application process, time-limited support and the potential for self-sustainability over the longer term. To date there have been three rounds funding 29 special facilities including biospecimen and data repositories, computational facilities and disease/attribute registries.² This highlights an important feature of the ATR in that it is not a private resource generated by a group of researchers for use in a particular study or program. The ATR does not undertake research itself, but acts as an enabler of research open to all researchers, including those who have not previously conducted twin studies.

Governance and Administration

The ATR is administered through The University of Melbourne and managed by a Director, John L. Hopper and Deputy Director, Susan A. Treloar. Under the requirements of the NHMRC Enabling Grant Committee, the governance structure and access policy of the ATR has been reviewed. An independent Advisory Board was instituted in 2005, chaired by one of the ATR twin members, and functions under an agreed Charter (see www.twins.org.au). The Australian Multiple Birth Association (AMBA) has accepted the ATR's invitation to nominate one of its members to the Advisory Board.

Use of the ATR by Researchers

The ATR welcomes approaches by all researchers and encourages researchers in Australia in all social science and health disciplines to understand the value of twins in

research designs, and learn about twin studies as a means of understanding epidemiological and clinical problems with a genetic and environmental perspective. Results can often be generalized to the wider population.

Use of the ATR is governed by established guidelines and procedures developed to comply with institutional policies, privacy legislation, and community and member expectations. These allow all Australian researchers access to its service on a fair, reasonable and equitable basis and are published on the ATR website (see 'Information for Researchers' at www.twins.org.au). Researchers are required to submit an 'expression of interest'. This allows initial timetabling and discussion around feasibility. The ATR can provide 'in principle' approval which can be referenced in funding applications. This prior consultation is strongly encouraged as an award of funding does not obligate the ATR to approve its use. ATR staff can assist researchers writing grant applications, ethics applications, and approach and information resources for delivery to potential twin-pair participants. No-one with a conflict of interest is involved in decision-making about access for a particular study.

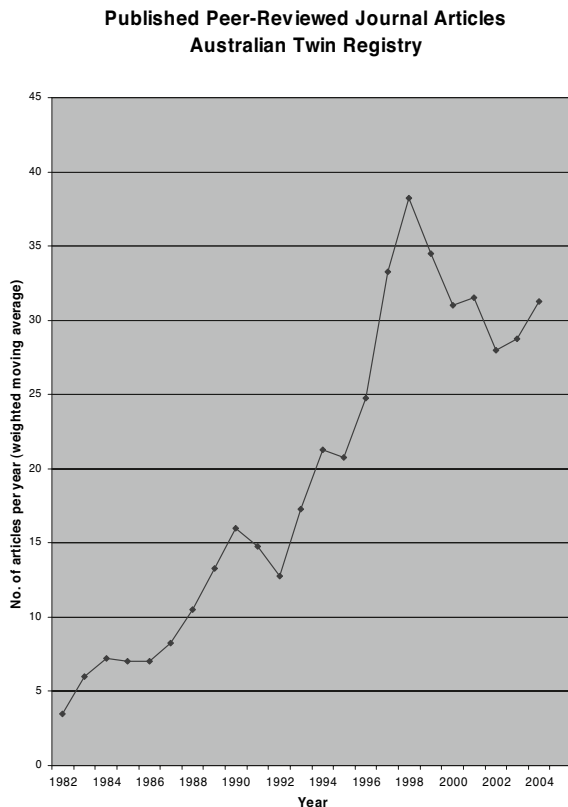
Recruitment of study participants can commence once ethics approval is completed. The initial approach is handled by the ATR. Given the commitment made to twins or parents when they register, that information is kept strictly confidential and that personal details are not given out without the prior consent of the individual concerned, researchers are provided with identifying information for a particular study only if and when the informed written consent of twins (or a parent) has been obtained. ATR staff work closely with researchers to ensure the best possible response rates by providing clear and consistent information about the study's aims and requirements. Researchers are required to reimburse ATR for direct costs (i.e., material and labour expenses) associated with recruitment for their individual projects on a cost-recovery basis. Over the last 4 years the ATR has conducted over 180 mail-outs comprising more than 80,000 letters. As shown in Figure 1, the rate of peer-reviewed publications has increased steadily since foundation and in recent years has averaged about 30 per year. A full bibliography is available on the ATR website.

When a study is completed and the data checked and cleaned, the ATR requests a copy of the data for its archives. The ATR is also working to offer the capacity to back-up biospecimen samples collected by projects in a biobank; see below. Researchers will be able to place conditions on third party access to their data and biospecimens

Current Aims

Through the new 5-year infrastructure funding, the ATR has:

- expanded its core operation by appointing additional staff supporting a wider scope of activities that enhance capacity to more effectively deliver services

**Figure 1**

The number of peer-reviewed publications per year (as a weighted moving average) from 1982 to 2004.

- appointed a paid part-time deputy director
- established an advisory board comprised of independent community stakeholders in order to advance the aims of the ATR and tap into the wide-ranging potential and diverse expertise of Australian twins and parents of multiples
- integrated with existing and newly developed population-based twin registers, the Western Australian Twin Child Health cohort (WATCH; Croft et al., 2002) and the Western Australian Twin Registry (WATR; Lee & Palmer, 2006)
- supported the establishment of a prospective population-based cohort of twins recruited during pregnancy (mothers and twin children — **match**)
- facilitated the training and development of Australian researchers by continuing to hold scientific workshops, fostered an active network of researchers from a range of disciplines, provided financial support for new researchers to attend international twin research workshops and conferences, and promoted the presentation of ATR studies at scientific conferences
- improved services to members, including annual Newsletters, regular Twin Festivals, and an expanded website.

In addition, the ATR is:

- enhancing community relationships and the ATR's public profile
- developing networks and proposals for commercial partnerships to support the ATR and twin research projects
- consolidating the electronic archiving of research data compiled from completed and ongoing ATR-supported studies to make these available to other researchers
- establishing a biobank of DNA and other biospecimen samples collected from previous studies (Note: This is related to project collection, not the generic collection of DNA).

Population-Based Cohorts

The ATR has in the past relied on voluntary recruitment, but is aware that, for some studies, this may introduce an ascertainment bias. Recent initiatives, financially and intellectually supported by the ATR, have addressed the need for population-based sampling.

WATCH Cohort and WATR

WATCH is Australia's first population-based twin and family cohort. It consists of 4719 families who had one or more multiple births in Western Australia between 1980 and 1995 inclusive, identified from the Maternal and Child Health Research database, which is housed at the Telethon Institute for Child Health Research in Perth (Croft et al., 2002; Hansen et al., 2004). Data were initially collected from 2355 families, with 13,000 individuals and 1647 families completing extensive baseline questionnaires, 708 an abbreviated asthma-specific questionnaire and 400 a language development study. This was extended in 1997, and now 5459 multiple births (11,189 children) have been identified. Over 90% of families have been traced and contacted; 79% have replied, and 88% of these have agreed to participate. Records are linked to routine data sources, providing data on maternal and perinatal factors, some postnatal complications, deaths and all hospital admissions during childhood. Core funding, administration, and use of WATCH have been incorporated within the ATR to allow sustainability, prevent duplication of recruitment, and combine expertise.

WATR extends WATCH to include adults born between 1974 and 1979, and children born from 1998 onwards. WATR will continue to enrol new birth year cohorts of multiple births indefinitely. This will produce the only population-based register of Australian multiples willing to participate in research studies (Lee & Palmer, 2006).

match Multiple Birth Pregnancy Cohort

The aim of **match** is to recruit, as an integral part of the ATR, on an on-going and national basis, a large cohort of mothers and their new born twins as a resource for

future research in twin pregnancy, genetics, epigenetics and other rapidly evolving areas, addressing the role of factors around the time of conception and during gestation as determinants of maternal and fetal health and fetal development. **match** will collect data on infertility and its treatment (Schieve et al., 2004; Johnson 2005), polycystic ovary syndrome and its treatment (Glueck et al., 2002), chorionicity (placentation), intrauterine environment including maternal prepregnant size, nutrition, hormonal status and exposure to medication, alcohol or other substances, as well as environmental factors. Antenatal data and biospecimens (maternal and cord blood) will be collected to allow researchers to measure factors relating to both shared and individual intrauterine environment.

Recruitment will be undertaken, using the help of midwives and obstetricians working in antenatal clinics, by providing all women recognized via ultrasound as having a twin pregnancy with a **match** 'twin pregnancy' folder that contains:

- booklets with information about twin pregnancy and support sources, prepared in consultation with a wide range of health professionals and parents of twins from AMBA
- an invitation to participate and a consent form for **match**
- a record book that comprises an initial questionnaire relating to maternal and paternal factors (the latter optional), conception, obstetric history, and factors up to conception, a questionnaire about ultrasound scans (and request to collect data prints), a questionnaire relating to pregnancy and delivery, a notes section (including pages for mothers to record the twins' family tree), blood sample collection forms, forms to report loss of a baby or revocation of consent, and an envelope to collect mementos.

match will mail out kits for blood collection (maternal blood sample taken at 28 weeks at the same time they have a routine blood sample taken, and cord blood samples from the twins, taken from the part of the cord left attached to the placenta after it has been cut). Mothers will be asked to complete the record book during pregnancy and after delivery, and can keep the book after delivery, returning the self-duplicating tear-out pages to **match** in prepaid envelopes provided.

Promotion of the ATR to the Wider Research Community

The ATR has traditionally run scientific workshops of interest to researchers under the title *It Runs In The Family*. These promote the exchange of ideas, encourage the creation of collaborative research groups, offer training in twin research methodologies, and provide networking opportunities for new researchers. These are continuing in different forms, run within or alongside medical research meetings. The ATR is also staffing exhibits at other research meetings so as to bring itself to the attention of a wider audience.

Network of Researchers

The ATR is continuing its development of an open, professional network of current and prospective researchers from a range of disciplines, with communication through e-mail announcing publications, conferences, collaborating opportunities, employment and funding opportunities, and so forth.

ATR Research Archive and Biobank

The ATR has baseline demographic and general health data, collected in 1982, between 1984 and 1992, and 1997, and is planning to archive other past studies. Researchers will be able to use and access a consolidated electronic archive of data compiled from completed and ongoing studies. The ATR is also establishing a biobank of DNA samples and other biospecimens collected from studies, including a central inventory of existing biospecimens stored in other laboratories.

Travel Awards

The ATR has instituted an Annual Travel Award Grant Scheme. It invites applications for awards on a twice yearly basis to assist with travel for students and postdoctoral fellows to attend training workshops or present results of twin research at national and international meetings.

Twins Newsletter

The Twins Newsletter is the ATR's main way of maintaining contact with members and publicising the work of researchers in the community. It includes communication regarding ATR activities, feedback about studies, accessible information about twin resources, and opportunities for contact between twins. Now generated on an annual basis, 50,000 copies are mailed to all adult members and the parents of young twins.

Twins+ Festival

In March 2006 the ATR collaborated with AMBA to host a national Twins+ Festival in Canberra (Figure 2). This was an opportunity for families with young twins and multiples, and for adult twins also, to get together and celebrate. The Festival was also an opportunity for the ATR and many research groups to staff exhibitions and engage with the twins, highlighting areas of their research and showing their appreciation for the massive contribution Australian twins have made to research. The hundreds of twins and other multiples who attended were aged from a few months old to over 90 and came from all over the country. They were entertained by a variety of performers and participated in a range of activities. Media coverage was excellent.

Website and Branding

The logo of the ATR has been an important unifying tool. It features elements recognizable to twins in

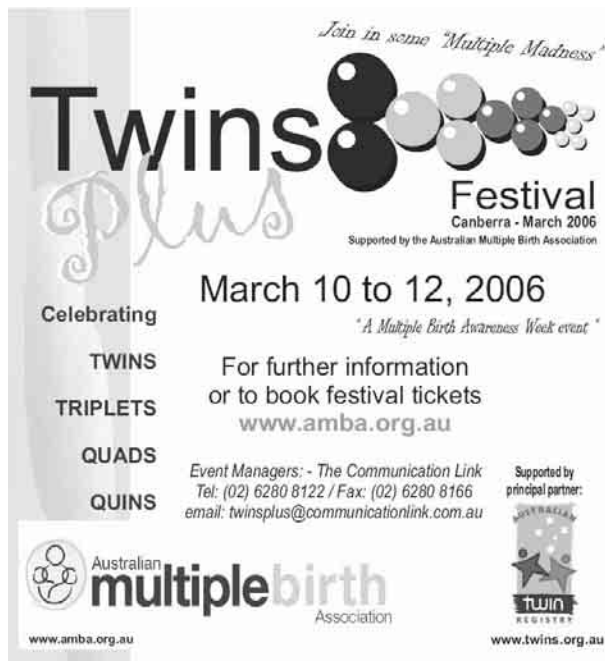


Figure 2

Flyer for Twins+ Festival held March 10–12, 2006 in Canberra, Australia's national capital city, as part of Multiple Birth Awareness Week. The Festival hosted an exciting range of activities for multiples and their families and was run in collaboration with the Australian Multiple Birth Association.

Australia and overseas — the Southern Cross (five stars), the blue ocean surrounding the continent, the yellow sandy beaches and the red deserts of Central Australia, and of course the 'stars' of the Registry, a pair of twins (see Hopper, 2002).

The ATR website www.twins.org.au has now been expanded and improved. Through the site, researchers can access the Research Application Kit, including application form in PDF format, and information about ATR workshops. Twins can access information about studies, copies of the Twins Newsletter, information sheets, registration form and photographs taken at ATR events.

Conclusion

Guaranteed 5-year funding from the NHMRC has allowed the ATR to develop, modernize and improve its procedures and infrastructure so that it can continue to play a major role in Australia's national research capacity. This funding has enabled the ATR to commence a range of new developments while continuing its major role in supporting longitudinal and cross-sectional studies involving twins well into the future. Consistent with its Mission Statement, the long-term goal of the ATR is to make twin studies a standard component of medical and scientific research.

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Endnotes

- 1 <http://www.health.gov.au/internet/wcms/publishing.nsf/Content/hmsr.htm>
- 2 <http://www.nhmrc.gov.au/funding/funded/outcomes/enableactiv.htm>

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