

DIRECTOR'S REPORT



Welcome to the 2007 Annual Report of the Australian Twin Registry (ATR). This new reporting style presents the work of the ATR in a more accessible format for two of our key stakeholder groups; twin members and the researchers we collaborate with.

The ATR is now over half way through the five year Special Facilities Enabling Grant awarded by the National Health and Medical Research Council (NHMRC) in July 2004.

This report summarises the project management and activities of the ATR during Year 2 and Year 3 of the grant (mid 2005 to mid 2007). It also summarises several of the major twin research programs underway in Australia facilitated by the work and resources of the ATR and the commitment of its members and their families.

The previous 2005 Director's Report highlighted the dedicated and productive work of a range of research scientists and projects supported by the ATR. This is an area which has expanded considerably over the last two years with a greater focus on studies of relevance to the health and welfare of all Australians. Throughout this time, the ATR has continued its mission to broaden its appeal and utility to researchers. Evidence of this is the diversity of research enquiries and Expressions of Interest we continue to receive.

Over the last few years there has been a lively and productive debate over the most suitable model for governing the ATR. Through the hard work by all involved, we are now enjoying the guidance of an independent Advisory Board, and the professional input of an Expert Reference Group of eminent scientists and

researchers that the ATR is able to call upon for advice and support.

As Director of the Registry for the past seventeen years, I have assisted in the ATR's growth and development with the help of some notable mentors, such as the Reverend Professor Graham Griffin, Professor Geoff Tregear AO, Professor Warwick Anderson AM, now CEO of the NHMRC, and more recently Vince Pollaers, who is the first lay Chair of the ATR Advisory Board. As Director, my aim is to ensure there is a robust, fair and transparent system of governance and procedural functioning to underpin the activities of the ATR well into the future.

Having guaranteed 5 year funding from the NHMRC has allowed the ATR to develop, modernise and improve its procedures and infrastructure so that it can continue to play a major role in Australia's national research capacity. Together with the dedicated support of a team of administrative staff, 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. Consistent with its Mission Statement, the ATR is continuing to encourage the use of twin studies as a standard component of medical and scientific research to improve the health and well-being of Australians.

John Hopper



CHAIRMAN'S REPORT



On behalf of the Advisory Board it gives me great pleasure to commend this report to you. Over the period to which this report relates, I have had the opportunity to work closely with, and observe, the management team of the Australian Twin Registry. I have been very impressed with what I have seen. It is remarkable the management team has been able to achieve given the limited funding and resources that it has available. It is clear to me that every member of the team truly believes in the importance of the Registry in supporting medical research in Australia.

The management team is mindful that all of its efforts would come to nothing if not for the support of its key stakeholders. On behalf of the management team and the advisory board, I would like to thank each of the twin and related family volunteers, the researchers using the facilities of the registry, and the University of Melbourne and National Health and Medical Research Council (NHMRC) for their continued support.

Finally, I would like to thank all of the individuals both past and present who have given of their time freely to support the Australian Twin Registry through involvement in past Executive Committees, the Advisory Board or the Expert Reference Group. The Registry looks forward to your continued support.

Vince Pollaers

Chair, ATR Advisory Board

ATR OVERVIEW

The Australian Twin Registry (ATR) is an important national and international resource for medical and scientific research across a broad range of disciplines. It was established in the late 1970s as a national volunteer registry of Australian twin pairs of all zygosity types and ages who are willing to consider involvement in health and medical research studies. Twins and Higher Order Multiples (HOMs) including triplets, quadruplets, and quintuplets are eligible to join regardless of their sex, age, place of location, health or medical history. The ATR currently manages information from more than 30,000 enrolled twin pairs and HOMs, and provides researchers with access to twin pairs suitable for specific studies once proposals are approved and twins have agreed to participate. The management of access to the resource enhances research capacity within Australia in a fair and equitable manner while protecting the rights of twins.

The ATR is a valuable resource for a wide range of quantitative and qualitative studies including:

- studies of genetic, epigenetic and environmental causes of variation in traits, and of susceptibility to disease
- co-twin control studies, using pairs discordant for disease or for measured exposure or genotype, to study the effects of measured environmental and genetic factors on disease outcome and measures of morbidity
- intervention studies matching for age, sex, and genetic factors
- longitudinal studies of the natural history of medical, physical, and behavioural characteristics
- studies related to twinning and to particular issues facing twins such as: clinical and service provision in twin pregnancies; maternal issues in pregnancy and after delivery; learning difficulties; the inheritance of twinning; the roles of chorionicity and placental factors, and of factors associated with sub-fertility and its treatment, as determinants of later health and neurodevelopment; and bereavement issues.

As an openly shared resource, the ATR provides researchers with access to an established infrastructure, a network of scientists, and administrative staff who are experienced in twin research. Current studies

utilising the ATR are run by a wide range of researchers from Australian institutes. Some studies are conducted in collaboration with overseas researchers.

The ATR's mission is to facilitate medical and scientific studies that involve at least in part the participation of twin pairs, and which use the special features that arise from twin study designs, to enable questions about health and well-being to be answered in ways that they otherwise could not.

This enables researchers to study the impact of genetic and environmental factors on health, and on the treatment and prevention of disease, including also those of particular relevance to the health and well-being of twins themselves. Results of twin studies are generally applicable to the wider community and ultimately result in the improved health and well-being of Australians.

FUNDING

The ATR is supported by an Australian National Health and Medical Research Council (NHMRC) Enabling Grant for the period 2004-2009. This new grant scheme responds directly to the recommendations of the Wills Report* and provides support for specific facilities that 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**. 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.

* <http://www.health.gov.au/internet/wcms/publishing.nsf/Content/hmrsr.htm>

** <http://www.nhmrc.gov.au/funding/funded/outcomes/enableactiv.htm>



ATR OVERVIEW

(continued)

VALUES

The following values guide the ATR in achieving its core functions:

Respect: The ATR conducts its operations with the fullest respect for the volunteerism of the twins and their relatives in their registration and participation; for the ATR staff in monitoring and maintaining the use of this resource; and, for the researchers in their efforts to conduct timely and relevant studies in accordance with their commitments to their funding bodies, made with the agreement of the ATR.

Leadership: The ATR will maintain and expand its role as an independent facilitator of twin studies, in training and informing researchers about the potential, design, conduct and analysis of twin studies, and in providing information about issues of relevance to twins.

Equity of Access: The ATR undertakes its functions under the principles of equity of access by researchers irrespective of factors such as institution, discipline, and relationship to ATR, and equity of participation of twins eligible for particular studies and activities.

Privacy and Confidentiality: The ATR holds information on registered twins in strictest confidence and in accordance with Australian legislative requirements.

Consumer Participation: The ATR engages in and conducts activities, with the twins and parents of twins whenever appropriate, whether or not they are members of the ATR.

Excellence in Research: The ATR strives to help researchers achieve excellence in their research.

The ATR does not undertake research itself but acts as facilitator. The ATR's core functions are:

Core Function 1:

Continued building and maintenance of an up-to-date database containing contact details and baseline information for twin members willing to participate in research

Core Function 2:

Collaboration with researchers applying to the ATR to ensure that projects are of significant scientific merit and are appropriately described to ensure potential participants are able to provide informed consent

Core Function 3:

Judicious management and administration of approach to eligible twin members to inform them of a new research project, determine their interest in participation, and seek their permission to release their contact details to the researcher

Core Function 4:

Development of projects and programs to value-add to twin research in Australia

Core Function 5:

Governance of the ATR in a fair, transparent and equitable manner

THE REGISTRY

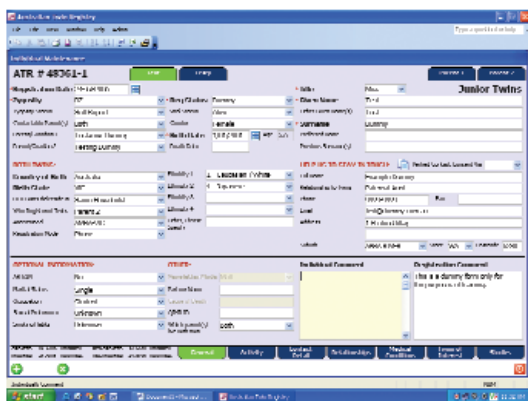
Continued building and maintenance of an up-to-date database containing contact details and baseline information for twin members willing to participate in research

THE REGISTRY AT A GLANCE – THE DATABASE

A foundation component of the Australian Twin Registry is the development and maintenance of an up to date register of twins willing to consider involvement in scientific studies.

Underpinning this register is the database tool used to store, retrieve and up date membership data to allow accurate record keeping and meaningful analysis of trends and results.

During 2005 the ATR Database Manager, Ms Kelly Aujard, together with the ATR Administration team developed a network-protected relational database with an SQL back office and Microsoft Access interface. The new database was launched in January 2006 and integrates the previous system which functioned with 3 separate databases. The new database enables improved consistency and more detailed data recording, including the ability to record all interactions with members.



A major feature is the automation of processes within the database, and ability to generate sophisticated reports to analyse a range of issues such as participation in studies stratified across age or location.

The ATR maintains information regarding contact details, date of birth, medical conditions of interest and zygosity. The database is held on a secure server at The University

of Melbourne. The ATR also requests the name and telephone details of a third party / next of kin who does not reside with the member, for the sole purpose of assisting in tracing members who have moved locations. The ATR requests that the twin inform their third contact of their inclusion on the ATR database. Third contacts are not utilised for any other purpose other than as a last resort if the ATR has lost contact with the twin pair.

Members remain registered until they request their permanent removal by phone, fax, mail or email. Members may make special requests regarding their consideration for studies, and can refuse to participate in specific studies or in all studies on a temporary basis, while still remaining on the ATR.

THE REGISTRY AT A GLANCE – MEMBER STATUS

The Australian Twin Registry Database currently holds details for 34,645 sets of twins and triplets. Of these, 28,557 (82.5% - 28,377 twin sets and 180 triplet sets) are willing to consider involvement in research studies.

Members of the Australian Twin Registry are recorded under a specific status, depending on the currency of their contact details and individual preference for involvement in research activities. This status defines the way in which the ATR interacts with the member, and therefore an important indicator of the availability of twins for different research activities.

If correspondence mailed to a member is returned to the ATR as a Return To Sender, the member is recorded as "pending" to prevent further mailings until such time as the member can be traced.

If the ATR has unsuccessfully attempted to trace the member they are recorded as "lost". If a member has informed the ATR that their co-twin is deceased, this does not preclude the surviving twin remaining on the register. Surviving twins may remain "Active" for studies, such as those involving bereavement, and can continue to receive the *Twins* newsletters.



2007 THE REGISTRY

Continued building and maintenance of an up-to-date database containing contact details and baseline information for twin members willing to participate in research

Table 1: Status Types

Status	Description
<i>Active</i>	Member willing to be approached for potential participation in research studies
<i>Deceased</i>	Member known to have passed away
<i>Duplicate</i>	A duplicate record
<i>Lost</i>	Unable to be located after attempt to trace via White pages, Electoral Roll and all contacts associated with database record
<i>Lost (O/S)</i>	Member was living overseas, now unable to be located after attempt to trace via Electoral Roll and all contacts associated with database record
<i>Newsletter</i>	Member not interested in participating in studies at this time, but interested in remaining on register and receiving newsletter
<i>Inactive</i>	The member has requested to be taken off the registry and does not wish to receive any further correspondence
<i>Overseas Temp</i>	Member or family have reported that the member is temporarily overseas, but still interested in remaining on register. Excluded from approach. Note, those overseas for a longer period of time and reside in the same location, can alternatively select <i>Questionnaire Only</i> status.
<i>Questionnaire Only</i>	Member willing to be approached for potential participation in questionnaire based studies only – unable to attend appointments and/or provide biosample/s
<i>Pending</i>	Return To Sender received for the recorded address, waiting on tracing, excluded from approach until reinstated as <i>Active</i> or <i>Questionnaire Only</i>

The current status of members of the Australian Twin Registry is summarised in the following table as at 30 June 2007. For reporting simplicity, triplets have been excluded from this table. The majority (82.5% - 28,377) of twin pairs are Active/Active (27,984), Active/Questionnaire (341) and Questionnaire/Questionnaire (52), indicating that they are willing to consider participation in research.

Table 2: Twin Pair Status Combination as at 30 June 07

Please note: Triplets excluded from table

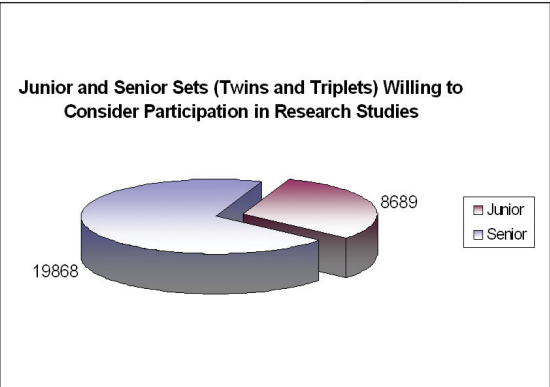
	Active	Dec'd	Duplicate	Lost	Lost (O/S)	N'letter	Inactive	O/S Temp	Q'aire	Pending	Total
Active	27984										27984
Deceased	617	463									1080
Duplicate	0	2	210								212
Lost	72	10	0	789							871
Lost (O/S)	3	0	0	3	3						9
Newsletter	134	31	0	1	0	55					221
Inactive	536	308	0	7	1	19	1132				2003
O/S Temp	422	2	0	1	0	1	8	94			528
Questionnaire	341	7	0	2	0	0	0	5	52		407
Pending	534	24	0	17	0	4	27	10	12	457	1085
Total	30643	847	210	820	4	79	1167	109	64	457	34400

Members are also referred to as Junior (under 18) or Senior (18 or older). This is an important distinction with regards to mailing address and consent. All Senior twins and triplets are mailed to personally once they turn 18. For Junior twins and triplets, the parent or guardian is approached.

Table 3: Junior and Senior where status is Active/Active, Active/Questionnaire and Questionnaire/Questionnaire Status as at 30 June 07

Set	Junior	Senior	Total
Twins	8602	19775	28,377
Triplets	87	93	180
Total	8,689	19,868	28,557

Graph 1: Junior and Senior Status as at 30 June 07



THE REGISTRY AT A GLANCE – AGE, SEX, ZYGOSITY AND LOCATION

The following table and graph summarises Active and Lost twin pairs stratified by sex and zygosity. For reporting simplicity, triplets have been excluded from this table.

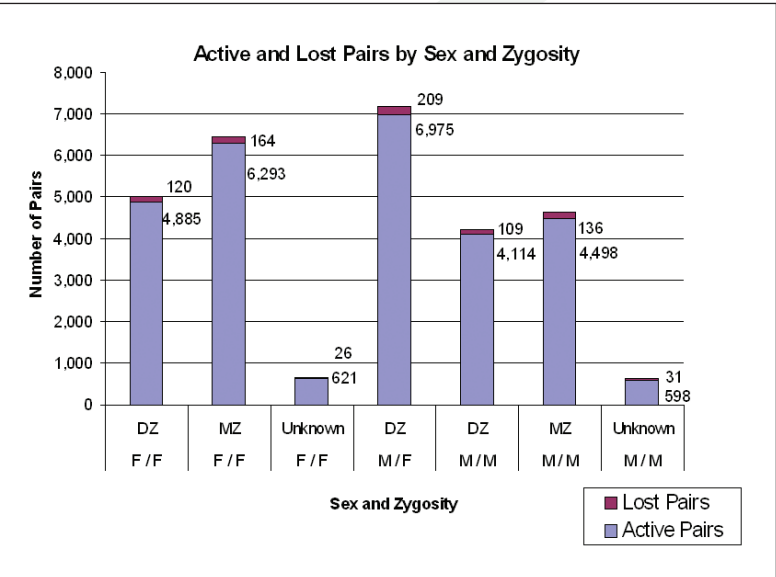
Table 4: Active and Lost Pairs by Sex and Zygosity

Please note: Triplets excluded from table

Sex	Zygosity	Active Pairs	Lost Pairs
F / F	DZ	4,885	120
F / F	MZ	6,293	164
F / F	Unknown	621	26
Total		11,799	310
M / M	DZ	4,114	109
M / M	MZ	4,498	136
M / M	Unknown	598	31
Total		9,210	276
M / F	DZ	6,975	209
Total		6,975	209
Total pairs		27,984	795

Graph 2: Active and Lost Pairs by Sex and Zygosity

Please note: Triplets excluded from graph





2007 THE REGISTRY

Continued building and maintenance of an up-to-date database containing contact details and baseline information for twin members willing to participate in research

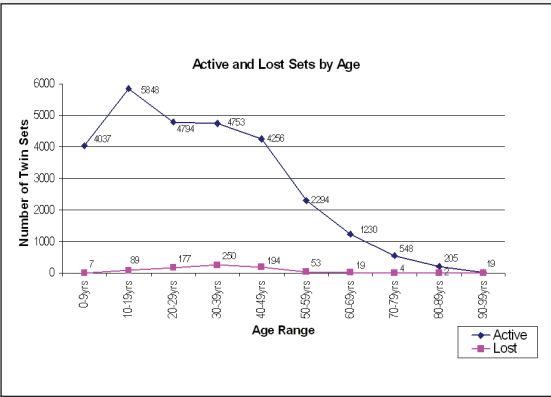
The following table and graph summarises Active and Lost twin pairs stratified by age and status. Of those who are Lost, the majority are in the age groups 20-29, 30-39 and 40-49 years. For reporting simplicity, triplets have been excluded from this table.

Table 5: Active and Lost Twin pairs by Age
Please note: Triplets excluded from table

Age	Active	Lost
0 - 9yrs	4037	7
10 - 19yrs	5848	89
20 - 29yrs	4794	177
30 - 39yrs	4753	250
40 - 49yrs	4256	194
50 - 59yrs	2294	53
60 - 69yrs	1230	19
70 - 79yrs	548	4
80 - 89yrs	205	2
90 - 99yrs	19	0
Total	27,984	795

Graph 3: Active and Lost Sets by Age

Please note: Triplets excluded from graph



The following table summarises the location of individuals, where both twins remain Active. In some situations, the twin's current location may be unknown (UNK) meaning that correspondence is directed either through the co-twin or parents. For reporting simplicity, triplets have been excluded from this table.

The labels 'Twin A' and 'Twin B' do not refer to birth order

Table 6: Active Pair Combinations by Location

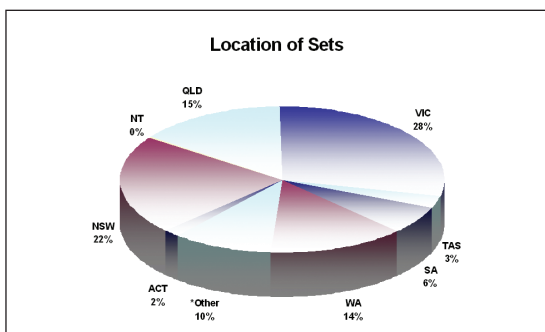
Please note: Triplets excluded from table

	Twin A											
Twin B	State	UNK	OS	ACT	NSW	NT	QLD	VIC	TAS	SA	WA	Total
	UNK	17										17
	OS	0	1									1
	ACT	1	1	498								500
	NSW	7	3	173	6081							6264
	NT	0	0	2	27	95						124
	QLD	8	2	56	447	32	4146					4691
	VIC	2	3	52	415	36	408	8055				8971
	TAS	2	0	16	51	6	44	73	776			968
	SA	4	1	19	93	26	90	156	14	1722		2125
	WA	4	3	18	99	20	87	169	22	51	3850	4323
	Total	45	14	834	7,213	215	4,775	8,453	812	1,773	3,850	27,984

The majority (90%) of twin pairs reside in the same state as one another, with Victoria and NSW providing the greatest proportion of registrations (50%).

Graph 4: Active Twin Pairs Combination by Location

Please note: Triplets excluded from graph



*"Other" defines pair residing in different states

This table summarises age and location where both twins reside in the same state. Twins and triplets residing in different states and/or overseas have been excluded for reporting simplicity.

Table 7: Active Sets Combinations by Location (those sets where twins/triplets live in the same state)

Range (years)	ACT	NSW	NT	QLD	SA	TAS	VIC	WA	Total
Twin Sets									
0 to 4	42	455	10	333	80	41	453	302	1716
5 to 9	54	523	14	387	124	63	630	510	2305
10 to 14	61	603	10	496	193	79	664	469	2575
15 to 19	71	830	21	649	184	114	906	490	3265
20 to 24	57	648	13	517	138	90	572	383	2418
25 to 29	51	550	10	448	112	80	611	364	2226
30 to 34	47	369	5	228	139	44	732	266	1830
35 to 39	29	397	2	212	231	42	944	340	2197
40 to 44	35	471	2	176	176	47	827	249	1983
45 to 49	21	338	1	176	86	77	514	182	1395
50 to 54	10	259	2	130	78	36	370	85	970
55 to 59	10	198	2	124	66	21	304	59	784
60 to 64	7	163	3	113	40	20	212	47	605
65 to 69	0	98	0	59	31	8	134	45	375
70 to 74	1	70	0	39	17	6	73	21	227
75 to 79	1	58	0	27	16	4	56	21	183
80 to 84	1	34	0	17	6	3	38	13	112
85 to 89	0	9	0	9	4	1	12	4	39
90 to 94	0	7	0	5	1	0	3	0	16
95 to 99	0	1	0	1	0	0	0	0	2



2007 THE REGISTRY

Continued building and maintenance of an up-to-date database containing contact details and baseline information for twin members willing to participate in research

Table 8: Active Sets Combinations by Location (those sets where twins/triplets live in the same state) continued

Range (years)	ACT	NSW	NT	OLD	SA	TAS	VIC	WA	Total
Triplet Sets									
0 to 4	0	5	0	8	0	0	3	6	22
5 to 9	1	9	0	6	1	0	7	5	29
10 to 14	0	2	1	7	2	0	4	7	23
15 to 19	1	12	0	6	2	1	6	4	32
20 to 24	1	6	0	3	2	0	3	6	21
25 to 29	0	3	0	3	0	0	6	3	15
30 to 34	0	3	0	3	0	0	4	3	13
35 to 39	0	2	0	0	2	0	3	0	7
40 to 44	0	1	0	0	0	0	3	1	5
45 to 49	0	0	0	3	0	0	1	1	5
60 to 64	0	0	0	0	0	0	1	0	1

RECRUITMENT

In order to maintain a vibrant and engaged register of twins, constant recruitment activities take place. As a result, 2,726 members (1,351 sets) joined the ATR during the two year period July 05 - June 07.

Graph 5: New Registrations (Sets) per Month

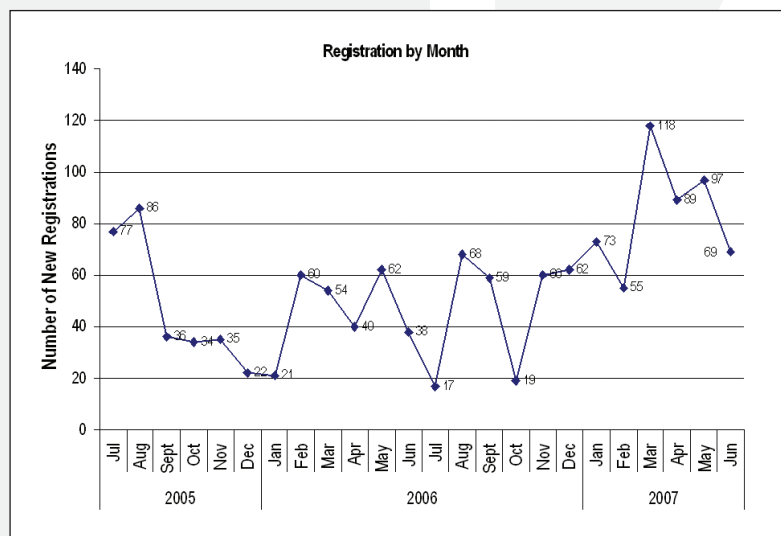


Table 9: New Registrations (Sets) per Month

Year	Month	Twins	Triples	Total
2005	Jul	75	2	77
	Aug	84	2	86
	Sept	35	1	36
	Oct	34	0	34
	Nov	35	0	35
	Dec	22	0	22
2006	Jan	21	0	21
	Feb	60	0	60
	Mar	53	1	54
	Apr	40	0	40
	May	62	0	62
	Jun	38	0	38
	Jul	16	1	17
	Aug	66	2	68
	Sept	58	1	59
	Oct	19	0	19
	Nov	58	2	60
	Dec	59	3	62
2007	Jan	72	1	73
	Feb	53	2	55
	Mar	115	3	118
	Apr	89	0	89
	May	95	2	97
	Jun	68	1	69
Total				1351

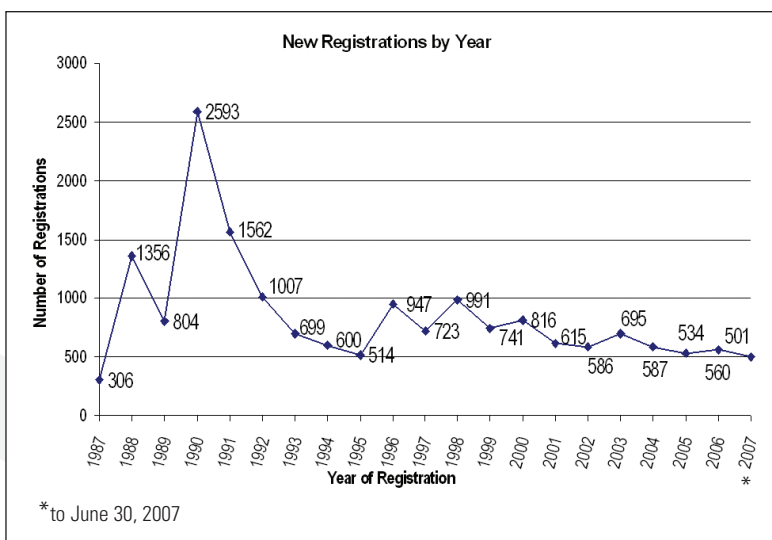
**Enabling Grant Goal:
Increase Membership by 5000 over 5 years**

The ATR aims to register 5000 new members during the period of the current Enabling Grant (July 1 2004 – 30 June 2009). Recruitment currently stands at 3,911 individuals (1,939 sets) for this period (78.2% of target). The launch of online registration via the ATR website has significantly increased registrations, with 1,011 members (501 sets) registering in the first half of the 2007 calendar year alone, which is almost double that of previous years. Plans are underway to significantly increase this figure during 2007/2008 by including incentive-driven recruitment campaigns directed at schools and via radio.

Table 10: New Registrations (Sets) by Year

Year	Twins	Triplets	Total
1986	16870	0	16870
1987	306	0	306
1988	1355	1	1356
1989	791	13	804
1990	2512	81	2593
1991	1544	18	1562
1992	1000	7	1007
1993	697	2	699
1994	598	2	600
1995	514	0	514
1996	945	2	947
1997	713	10	723
1998	987	4	991
1999	738	3	741
2000	806	10	816
2001	608	7	615
2002	582	4	586
2003	690	5	695
2004	577	10	587
2005	525	9	534
2006	550	10	560
1st half 2007	492	9	501

Graph 6: New Registrations (Sets) by Year



It is important to acknowledge that over the course of 20 years the great majority of new registrations have been received from parents with young multiples. The following table and graphs indicate that families with twins in the 0-9 years age group are receptive and enthusiastic stakeholders in new registrations, representing 67.5% of all new registrations.



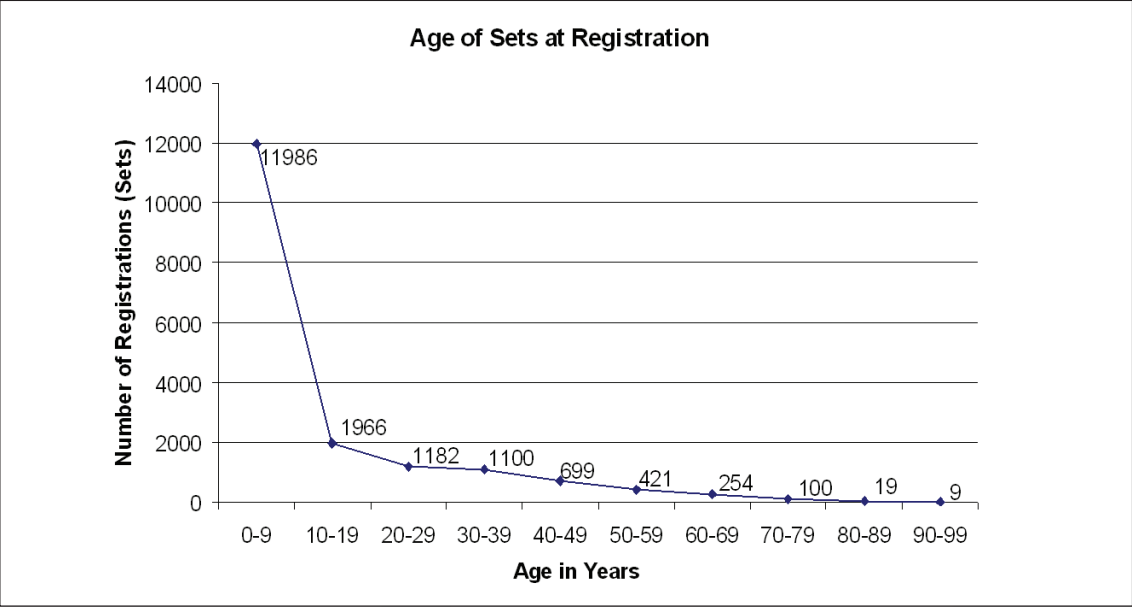
THE REGISTRY

Continued building and maintenance of an up-to-date database containing contact details and baseline information for twin members willing to participate in research

Table 11: Age at Registration

Year	0-9	10-19	20-29	30-39	40-49	50-59	60-69	70-79	80-89	90-99	Total
Twins											
1987	195	18	35	18	18	7	9	6	0	0	306
1988	679	180	174	154	74	60	27	6	0	1	1355
1989	572	48	79	51	21	8	11	1	0	0	791
1990	1243	345	236	293	196	93	70	28	7	1	2512
1991	866	164	161	148	103	47	40	11	3	1	1544
1992	565	198	76	74	37	19	19	8	3	1	1000
1993	469	93	35	33	32	16	13	5	0	1	697
1994	369	111	31	31	26	14	11	5	0	0	598
1995	390	64	21	17	9	9	3	0	1	0	514
1996	724	103	25	32	24	19	6	8	4	0	945
1997	557	66	28	25	15	17	3	2	0	0	713
1998	674	184	50	27	31	16	2	2	0	1	987
1999	578	58	22	30	13	26	7	2	1	1	738
2000	625	91	25	28	19	9	6	3	0	0	806
2001	520	22	18	19	9	15	4	1	0	0	608
2002	504	19	14	18	16	8	2	1	0	0	582
2003	524	60	45	27	15	16	1	2	0	0	690
2004	459	27	28	25	18	12	6	2	0	0	577
2005	427	33	27	14	8	4	5	5	0	2	525
2006	465	28	17	17	9	5	9	0	0	0	550
2007	438	18	16	14	3	1	0	2	0	0	492
Triplets											
1988	1	0	0	0	0	0	0	0	0	0	1
1989	10	1	1	1	0	0	0	0	0	0	13
1990	36	24	18	2	1	0	0	0	0	0	81
1991	10	5	0	0	2	0	0	0	0	0	18
1992	5	2	0	0	0	0	0	0	0	0	7
1993	0	1	0	1	0	0	0	0	0	0	2
1994	2	0	0	0	0	0	0	0	0	0	2
1996	2	0	0	0	0	0	0	0	0	0	2
1997	10	0	0	0	0	0	0	0	0	0	10
1998	3	1	0	0	0	0	0	0	0	0	4
1999	3	0	0	0	0	0	0	0	0	0	3
2000	10	0	0	0	0	0	0	0	0	0	10
2001	7	0	0	0	0	0	0	0	0	0	7
2002	4	0	0	0	0	0	0	0	0	0	4
2003	5	0	0	0	0	0	0	0	0	0	5
2004	9	1	0	0	0	0	0	0	0	0	10
2005	7	1	0	1	0	0	0	0	0	0	9
2006	10	0	0	0	0	0	0	0	0	0	10
2007	9	0	0	0	0	0	0	0	0	0	9
Total	11986	1966	1182	1100	699	421	254	100	19	9	17736
%	67.58	11.08	6.66	6.20	3.94	2.37	1.43	0.56	0.11	0.05	

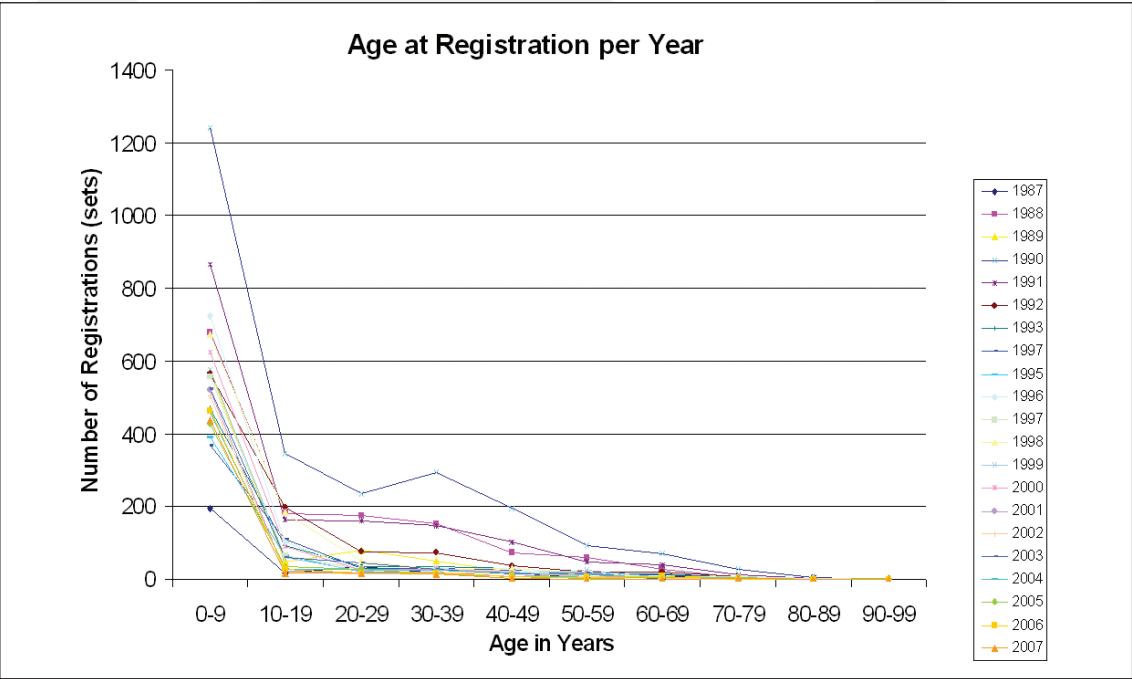
Graph 7: Age at Registration over the course of 20 years



The Age at Registration profile remains relatively consistent each year over a 20 year period. Of note is the trend seen in the large recruitment campaign undertaken in 1990, where a jump in registrations in all age groups was seen, especially in the age group up to and including 40-49 years. The flattened registration profile in the later age groups recently suggests that a recruitment campaign targeting older age groups may see significant successes in increasing registration.

Table 12: Age at Registration Each Year

Please note: Triplets excluded from graph





2007 THE REGISTRY

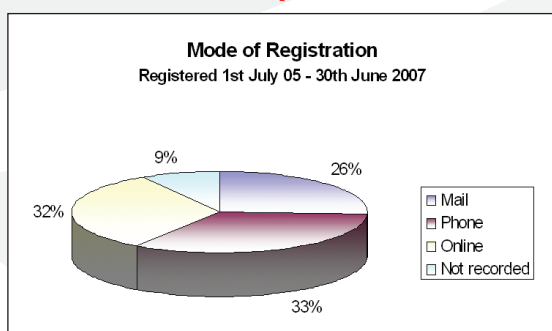
Continued building and maintenance of an up-to-date database containing contact details and baseline information for twin members willing to participate in research

New registrations are taken over the telephone, online or via mail.

Table 13: Mode of New Registrations (Sets) between 1 July 05 – 30 June 07

Mode of Registration	Registrations	%
Mail	348	26
Phone	454	33
Online	432	32
Not recorded	117	9
Total	1351	

Graph 7: Mode of New Registrations (Sets) between 1 July 05 – 30 June 07

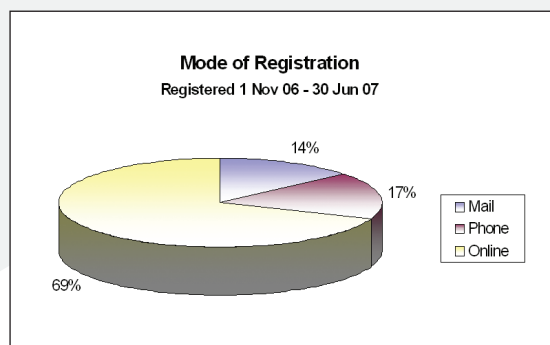


The majority of registrations for the period 1 July 05 – 30 June 07 have been via telephone. Since the launch of the new website and online registration system, online registrations have increased from 32% to 69% in proportion to other modes.

Table 14: Mode of New Registrations (Sets) since launch of new website online registration (1 November, 2006)

Mode of Registration	Registrations	%
Mail	85	14
Phone	107	17
Online	432	69
Total	624	

Graph 8: Mode of New Registrations (Sets) since launch of new website online registration (1 November, 2006)



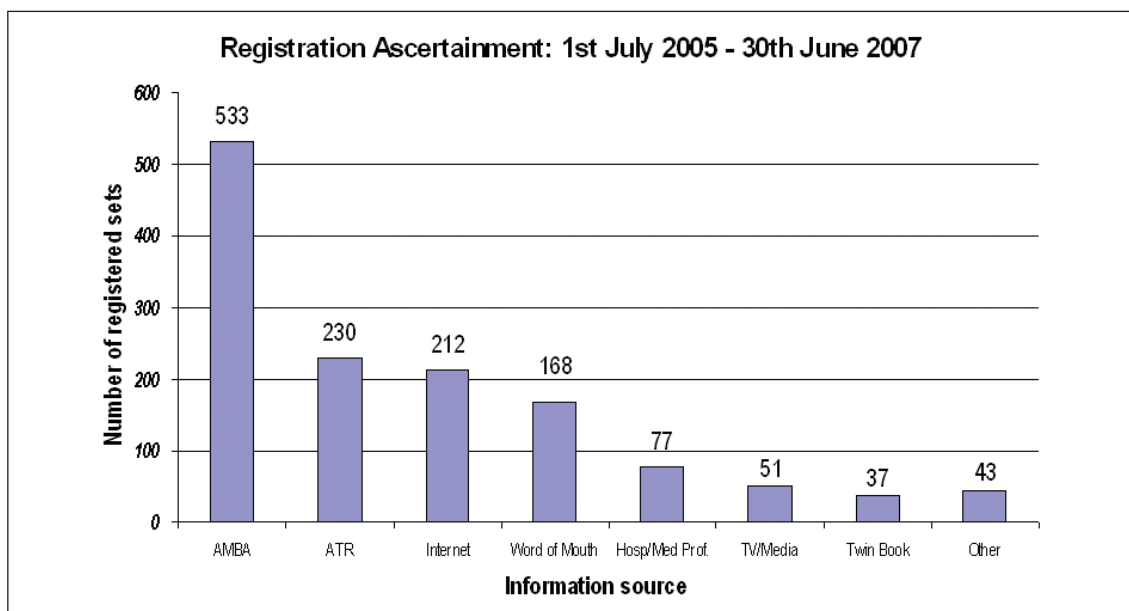
The ATR maintains a number of ongoing recruitment channels:

- Advertising with the Australian Multiple Birth Association (AMBA) online forum, website, e-journal and magazine
- Website
- Word of mouth
- Information provided by Doctor, Midwife, Hospital staff or Maternal and Child Health Care nurse
- Project specific advertising via radio, news release and print media
- Media opportunities such as participation in television shows, general comment on scientific progress
- Publications relating to twins where the ATR is mentioned and/or contributed
- **match**, WATR and WATCH

Table 15: Registration Ascertainment (Sets)

Information Source	Registrations	%
AMBA	533	39
Internet	212	16
Word of Mouth	398	29
Hosp/Dr/Midwife	77	6
TV/Media	51	4
Twin Book	37	3
Other	43	3
Total	1351	

Graph 9: Registration Ascertainment



RECRUITMENT ACTIVITIES

It is estimated that about 10 -15% of the total twin population of Australia are members of the ATR. This reflects the voluntary status of the register and is influenced by:

- public awareness of the ATR
- feelings toward medical research that each individual holds
- the requirement for both members of a twin pair to register
- availability of time and effort by each individual

Throughout the period July 2005 – June 2007 a number of promotional activities were undertaken by the ATR and researchers. These included; small print based articles in local media for a number of studies; presentations at local facilities affiliated with particular studies (such as the Schizophrenia Fellowship) and; radio and television interviews with researchers and participants. Where an ATR affiliated research project is underway that attracts twin participants who are not members of the ATR, the ATR asks the researcher to inform the twin pair about the facility.

The ATR also conducted the following recruitment activities:

- The ATR released a Video News Release via the University of Melbourne Media Unit, which is available as stock footage for future broadcasts.
- Promotion of the ATR through the SBS "Insight" program "Two of A Kind" September, 2006
- Booth at Australian Science Festival Canberra 17-21 August, 2005
- Paid Banner advertising on the Australian Science Festival 2005 website
- Booth at Medical Research Week, Melbourne, 5 June, 2005



*The Beynon twins participating in the WATCH for Asthma study
(Photo courtesy of Australian Multiple Birth Association)*



2007 THE REGISTRY

Continued building and maintenance of an up-to-date database containing contact details and baseline information for twin members willing to participate in research

The ATR and the Australian Multiple Birth Association (AMBA) have worked hard over the past 2 years to develop and strengthen the relationship between the two organisations, including the invitation of an AMBA representative to the ATR Advisory Board. This collaboration brings mutual benefit to both organisations and results in increasing goodwill between the organisations; sharing of resources and cost saving methods; co-branding to reduce promotional costs; and promotion of the registry to our key stakeholders – twins and families of twins.

Specific recruitment activities undertaken in collaboration with the Australian Multiple Birth Association (AMBA) include:

- Major sponsor of new AMBA initiative 'Bundles for Multiples'
- 1/4 page paid advertisement in e-journal June 2007 for studies of interest to young twins
- Full page advertisement in the Australian Multiple Birth Association (AMBA) magazine March and July 2006 (first and second edition of the magazine) introducing the ATR
- Full page advertisement in the Australian Multiple Birth Association (AMBA) magazine March 2007, highlighting online registration
- Participation and posting to the AMBA e-forum regarding studies of interest to AMBA families

NSW AMBA State Symposium

The ATR was invited to attend the NSW AMBA State Symposium in Wollongong in May, 2007. This was a good opportunity to meet local groups and encourage participation and garner support.

AMBA National Convention

The ATR has been invited to present a session on the service to AMBA members at the National Convention in Newcastle in November, 2007. This is an important opportunity to garner support across Australia.



CURRENCY AND ACCURACY OF MEMBERSHIP DATA – RETURN TO SENDER

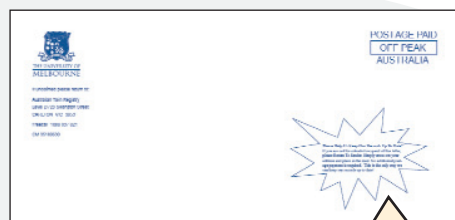
The ATR undertakes a series of activities throughout the year to maintain the accuracy of twin records, including the mailout of an Annual Twins newsletter. These types of activities generate Return To Sender (RTS) and Change of Address updates. Upon receipt of RTS, ATR Research Assistants trace the location of the twin member via other family members, third contacts, the White Pages or the Electoral Roll.

**Enabling Grant Goal:
Accuracy of Database over 85%**

Once a Return To Sender is received, the individual's database record is placed into Pending status. Pending Status figures are an important measure of the accuracy of the database. The ATR has a goal of maintaining Pending Status proportions below 15%

The ATR sent the 2005 *Twins* Newsletter to 50,912 households and received 1,054 RTS (2.07%) envelopes. All of these RTS were followed up prior to the 2006 *Twins* Newsletter mailout.

The ATR is aware that not all misdirected mail is in fact Returned to Sender, and as such the 2006 edition of *Twins* was mailed in an envelope bearing a distinctive message regarding the importance of returning misdirected mail:



Please Help Us Keep Our Records Up To Date!

If you are not the intended recipient of this letter, please Return To Sender. This is the only way we know our members have moved!

The 2006 edition was sent to 51,669 households and resulted in 2,932 RTS (5.67%). It is thought that the increase in RTS received for the 2006 edition is, in part, due to this envelope message.

CURRENCY AND ACCURACY OF MEMBERSHIP DATA – RECORD UPDATES

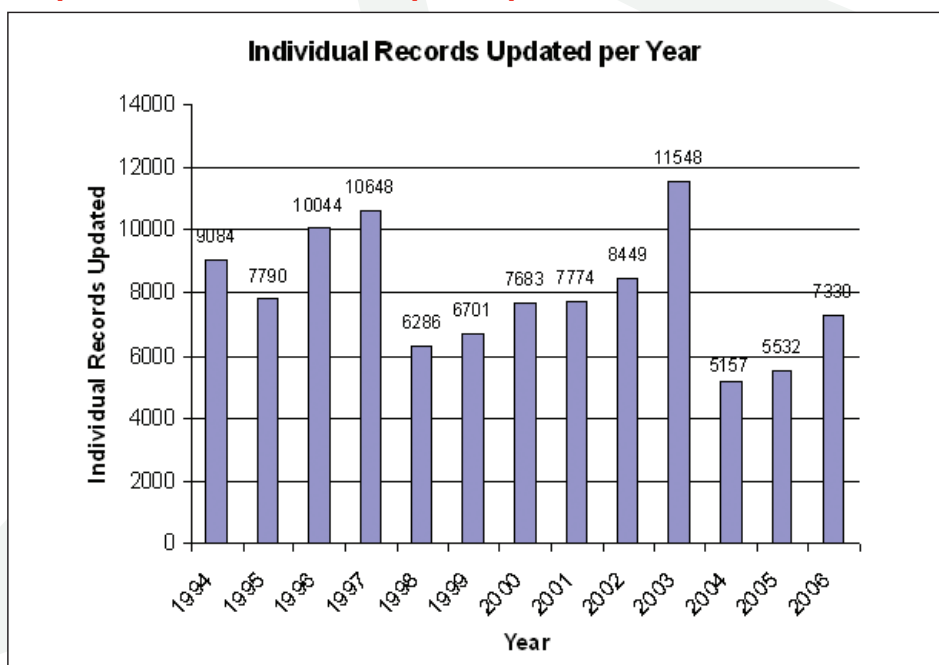
While RTS figures are important in determining the accuracy of the database, the ATR acknowledges that not all misdirected mail is in fact returned to the Registry. It is for this reason that proactive updates are also conducted for families who have not had direct contact with the ATR in the previous 3 years. This is an ongoing and important maintenance activity and ensures that the Registry remains viable.

All prior addresses and any actions taken to trace individuals are recorded on the ATR database.

During the period July 05 – June 07, 16,084 individual records were updated in the ATR database; 5,532 in 2005 and 7,330 in 2006.

Note that these figures include those records followed up due to receipt of an RTS.

Graph 10: Individual Records Updated per Year



CURRENCY AND ACCURACY OF MEMBERSHIP DATA – RECORD MANAGEMENT PROGRAM

The ATR instigated a record management program in 2006 to electronically archive all paper-based membership and response records. These records are the foundation of the Registry and physically record each member's consent and personal details. It is important that the records are retained in a robust and accessible system.

This effort was only achieved by the support and hard work of the University of Melbourne Imaging Centre at the Records Services department.

Over 131,564 pages of documentation were digitally archived over the course of 6 months, resulting in a resource that is now more accessible to ATR staff.

The ATR is now expanding the electronic archive to include all ATR Response Forms. This will reduce space requirements for archiving the documents and improve office systems to enable labour savings.



2007 THE REGISTRY

Continued building and maintenance of an up-to-date database containing contact details and baseline information for twin members willing to participate in research

MEMBER COMMUNICATIONS

Member communications are vital to promote willingness to participate in research and provide another avenue to return information and results to members who have already participated in studies.

Enabling Grant Goal:
Twins Newsletter to be published annually

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 articles regarding ATR activities, results of studies that are underway or completed calls for interest for additional participation for new and upcoming studies, accessible information about twin resources, communication regarding ATR administration and governance, features on twin research in Australia and opportunities for contact between twins. The newsletter is full colour 6 - 8pp A4 and is usually mailed annually.

The *Twins* newsletter is written in an informal and educational style so that twin members, their parents and other readers are engaged and learn about the scientific basis behind twin research and specific projects. It also profiles current researchers so that twin members can become more familiar with research associated staff.

The 2004 *Twins* Newsletter went out on 7 October, 2004 to 53,235 households, the 2005 *Twins* Newsletter went out on 23 November, 2005 to 50,912 households and the 2006 *Twins* Newsletter went out on 22 November 2006 to 51,669 households.

For copies of these editions and those of previous years, please see the ATR website at www.twins.org.au

Twins Plus Festivals

Enabling Grant Goal:
Convene two Twins Festivals

In March 2006, the ATR collaborated with the Australian Multiple Birth Association (AMBA) to host a national Twins+ Festival in Canberra. 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 1500 twins and other multiples who attended were aged from a few months old to over 90 and came from across the country. They were entertained by a variety of performers and participated in a range of activities. Media coverage was excellent.



The next Twins+ Festival is scheduled for 2009.

Website

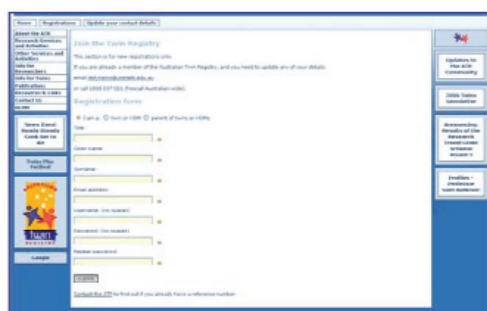
The ATR launched a new look website located at www.twins.org.au in November 2006, replacing the old website with a fresh design, greater interactivity and more information.

Enabling Grant Goal:
Develop a comprehensive website

The website is used to communicate news and information to twin members, researchers and others. This website also acts as a channel for recruitment and a clearinghouse for application documentation.



A new feature of the website is the ability for prospective members to register online. This has proved a popular channel for member recruitment with 432 sets (872 individuals) enrolling online in the first seven months after its launch.



Media Activities

The ATR is able to assist in recruiting twins for appearance on television/radio for requests that are deemed ethically appropriate and have a justifiable health and/or scientific basis. The media contact or network concerned is required to provide a list of eligibility criteria and a 'Letter of Invitation' which is sent to suitable twins together with an ATR Approach Letter. In general, the ATR prefers to utilise a letter-based approach but can provide a telephone-based approach if negotiated in discussion with the ATR Coordinator. The ATR does not, under any circumstance, provide the contact details for a twin, or twin family, directly to the media.

The ATR's preferred policy is to provide the relevant media contact details to members and allow interested twins, or parents (in the case of minors), to contact the media, rather than vice versa.

The media network concerned is asked to promote the ATR, including communication of the 1800 number, as part of the agreement to recruit or contact twins on their behalf.

The ATR charges a Fee for Service of \$10 per pair approached and \$60 per hour worked (price updated in November, 2006). These fees are invoiced after the approach, and the invoice is payable within 7 days.

Media activities in 2006-2007 included:

- SBS Insight: Two of a Kind: Tuesday 12th September on SBS 7:30pm - 8:30pm
Audience members
- Sony Cyber Shot commercial
Auditions

- Twins Ready Steady Cook 18th May 2006
(in collaboration with AMBA)

Twin members can register their interest in being contacted regarding media activities with the ATR.



ATR members Kathy and Karen and members of AMBA hamming it up for Ready Steady Cook (Photo courtesy of Australian Multiple Birth Association)

CAPACITY BUILDING – MATCH, WATCH AND WATR

Enabling Grant Goal:
Increase the capacity of the ATR to attract membership Australia-wide

The ATR financially supports 3 satellite projects; Mothers and Twin Children (**match**), the Western Australia Twin Children cohort (WATCH) and more recently, the Western Australian Twin Register (WATR), which act as embedded recruitment channels.

When twins are ascertained through these channels, they are either informed that they are automatically registering with the ATR (as is the case with **match** and WATR) or are provided with information regarding the ATR and can then register as ATR members if they choose (WATCH). Much work has been undertaken over the previous 2 years to strengthen links with these projects, and to continue the collaboration for mutual benefit.

match / WATCH / WATR / ATR WORKSHOP

The **match**, WATCH and WATR programs are key resources of the ATR. On March 13-14, 2007 the ATR held a productive workshop involving the ATR, **match**, WATCH and WATR management, to explore new ways of working together for the benefit of twin research. The workshop demonstrated a strong spirit of collaboration and alignment of interests. The workshop was viewed as a success by all.



2007 THE REGISTRY

Continued building and maintenance of an up-to-date database containing contact details and baseline information for twin members willing to participate in research

match REPORT

As an integral part of the ATR, the aim of **match** is to recruit, on an on-going and national basis, a large cohort of mothers and their new born twins. This cohort will be a resource for future research addressing the role of factors around the time of conception and during gestation as determinants of maternal and fetal health and fetal development. Recruitment to **match** will begin in 2007 and gradually roll out to hospitals and states across Australia.

match is collecting data and biological samples to measure periconceptional and intrauterine environment, including maternal pre-pregnant size, nutrition, lifestyle, hormonal status and exposure to medication, alcohol or other substances, as well as recording infertility and its treatment, and chorionicity (placentation). Stored cord blood will be available to facilitate research in genetics, epigenetics and other rapidly evolving areas.

Recruitment is on a volunteer basis; all women with a twin pregnancy will be provided with a **match** "twin pregnancy" folder. These have been printed following ethics approval from The University of Melbourne (being the overarching ethics body responsible for **match**) and the three main maternity hospitals in Melbourne; The Royal Women's Hospital; Mercy Hospital for Women and; Monash Medical Centre.

- 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), sample collection forms, forms to report loss of a baby or revocation of consent, and an envelope to collect mementos.

Women who decide to join **match** are asked to:

- complete the consent form and return it with the completed initial questionnaire
- use the kits that are mailed to them to ask staff to collect some of their blood at 28 weeks, (at the same time as they have a routine blood sample taken), and cord blood samples from their twins
- complete the record book during pregnancy and after delivery, returning the self-duplicating tear-out pages to **match** in pre-paid envelopes provided. This means they can keep the book as a record of their twin pregnancy

match undertakes education sessions to inform medical and midwifery staff about the project, and posters have been prepared for women expecting twins (telling them about the folder) and for staff, (telling them about types of twins, how to determine chorionicity and the protocol for blood sample collection and processing).

The **match** Twin Pregnancy Folder 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 **match** consent form



WATCH REPORT

WATCH (Western Australian Twin Child Health) is Australia's first population-based twin and family cohort. It consists of 4,719 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. Data were initially collected from 2,355 families, with 13,000 individuals and 1,647 families completing extensive baseline questionnaires; 708 an abbreviated asthma-specific questionnaire; 400 a language development study. This was extended in 1997, and now 5,459 multiple births, (11,189 children) have been identified. Over 90% of families have been traced and contacted; 79% replied, and 88% of these agreed to participate. Records are linked to routine data sources, providing data on maternal and perinatal factors, some post-natal 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 REPORT



(L-R) Professor Lyle Palmer, Co-Director of WATR, with members Blake and Lloyd Whiby

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.

The Telethon Institute for Child Health Research (TICHR) currently manages WATR registered child multiples born

1980-1997, and will manage the 1998+ births expansion, to commence in 2007. The recruitment of multiples born between 1974 and 1979 (referred to as "adult multiples") commenced in January 2006 by the Western Australian Institute for Medical Research (WAIMR).

THE WA DATA LINKAGE SYSTEM AND THE WATR

The WA Data Linkage System (WADLS), established in 1995, comprises over three decades of health data on the entire WA population. The core WADLS data are based on linkage within and between the WA statutory collections (all births, deaths, hospitalisations, midwives records, mental health and cancer registrations), Commonwealth data such as the PBS and MBS registers, and additional internationally unique population-based disease registries and health surveys.

In WA, records of women who have given birth in the state are held as a legal requirement by the Registry of Births, Deaths and Marriages. This information was released to WATR by the Registrar General of Western Australia after it was agreed that the use of the data would be of benefit to the community. As electronic health data currently in Western Australia dates back to 1974, all multiple births in WA since then were identified through maternal health data. These were linked with WA mortality data to identify which multiples had died, and siblings of these people were deemed ineligible for WATR recruitment to avoid unnecessary distress to families. All remaining names were then linked with the WA Electoral Roll to source addresses to contact eligible multiples. Using WADLS, WATR can identify eligible WA multiples and add data from 1974 to 1979, 1998 to 2004, and from 2005 onwards as the data become available.

Linkages are created and maintained through rigorous privacy protocols, probabilistic matching and extensive clerical review. This unique resource enables the study of total population longitudinal data and family record linkage in an unbiased way. The potential to link the core population-based datasets to twin cohort and family studies means that WATR has the ability to investigate the changing roles of genes, environment, gene-gene, and gene-environment interactions over the entire life span in population-based samples of twins.



THE REGISTRY

Continued building and maintenance of an up-to-date database containing contact details and baseline information for twin members willing to participate in research

RECRUITMENT OF ADULT MULTIPLES (1974 TO 1979 COHORT)

The recruitment of adult multiples began with a mail-out to all identified eligible multiples. This mail-out consisted of an invitation letter to join the Register, an information leaflet, consent form, registration form, reply paid envelope and an ATR newsletter. The registration form asked for demographic and basic twin family details (e.g. zygosity and presence of other twins in the family). The ATR newsletter was included with the aim of showing potential multiples examples of current Australian twin research. By registering, multiples were consenting to be contacted at a later date by researchers who may request their participation in future research studies. Participation in WATR is entirely voluntary, and multiples were informed that even if they register with WATR, they were under no obligation to participate in any future studies. All registrations were confirmed by letter or telephone call.

Follow-up calls were carried out for all eligible multiples that had not sent in a reply following the initial mail-out.

Their contact phone numbers were sourced through the White Pages, and telephone calls were conducted between 6-8pm on weeknights. When contact was made in this manner, multiples were reminded to send their consent and registration forms. If they no longer had them, they were given the option to register over the phone or have an invitation package resent to them. They were also directed to the WATR website where consent and registration forms could be downloaded. For potential participants who could still not be contacted, invitation packs were resent.

A total of 1407 adult multiples were identified from birth records as being eligible for contact for the 1974-79 extension of WATR. Only twin and triplet sets could be sourced, with no quadruplets or quintuplets being born in Western Australia during these years. For 250 sets of twins, contact details of only one twin could be sourced. Similarly, contact addresses for all three triplets could only be sourced for seven of the nine triplet sets – only two of the three triplets could be found for these sets (Table 1). This was due to the inability to source their addresses through the WA Electoral Roll. In such cases, the invitation letter was altered, requesting the contactable twin/triplet to invite their sibling to join WATR.

Table 16: Number of multiples born 1974-1979 eligible for contact for adult expansion of the WATR.

Multiple Group	No. multiples per group	No. multiple groups	Total
Twin Pairs	2	566	1132
Incomplete Twin Pairs	1	250	250
Triplet Sets	3	7	21
Incomplete Triplet Sets	2	2	4
Total			1407

Following a low response rate from the initial mail-out (n=256, 18%), potential participants were contacted by telephone after sourcing their telephone numbers from the White Pages. Seventy-six (5%) invitation packs were returned to sender, therefore their addresses were no longer current and therefore could not be used to source telephone numbers. Of the 1075 remaining multiples, 512 telephone numbers were sourced.

Of the 512 multiples to be contacted by telephone, contact was made with 392 multiples. Most were

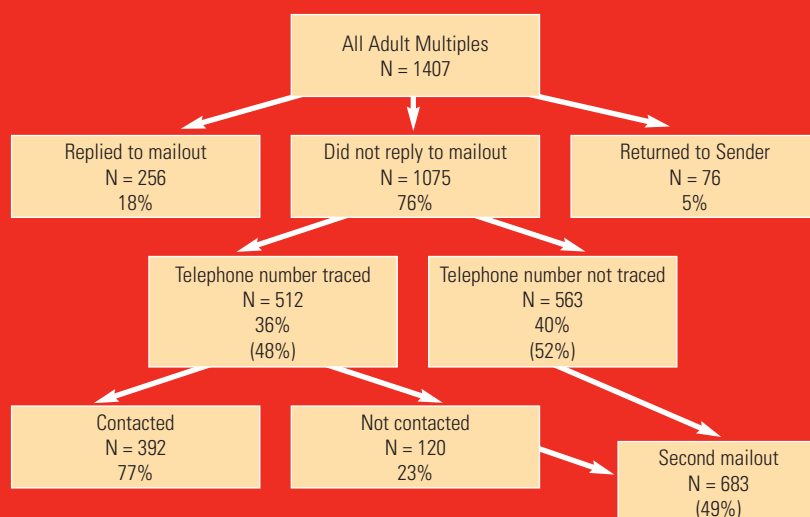
registered over the phone (n=151), 89 requested forms to be resent, 11 said they would send the forms back and eight preferred to be contacted at another time. One hundred and thirty-three multiples indicated that they were not interested. The remaining 120 were not personally contacted – messages were either left with a household member or answering machine, the caller was informed that they were away, or there was no answer. Three attempts were made where there was no answer (Table 2).

Table 17: Results of the follow-up phone calls to multiples born in 1974-1979 who did not respond to initial invitation.

Results of Phone Call (after all attempts made)	Number	%
Registered over the phone	151	29
Not interested	133	26
Asked to resend forms	89	17
Would send back forms	11	2
Preferred to be contacted later	8	2
Away	20	4
Left message	40	8
No answer	60	12
Total	512	100

A second mail-out was undertaken, targeting those that were non-responders following the initial mail-out, and could not be contacted via telephone (n = 683, 48%) (Fig 1).

Figure 1: The Western Australian Twin Register, 1974-1979



Active recruitment was completed at the end of 2006, by which time 507 adult multiples had registered, of which there are 144 complete twin pairs, and two complete triplet sets – an overall response rate of 36%.



SCIENTIFIC MERIT

Collaboration with researchers applying to the ATR to ensure that projects are of significant scientific merit and are appropriately described to ensure potential participants are able to provide informed consent

APPLICATION

The ATR welcomes applications from researchers in all social science and health disciplines. Dialogue is encouraged to promote understanding of the value of twins for research and to explore how twin studies may provide a means for understanding health and medical problems from a genetic and environmental perspective. Results can usually be generalised to the wider population.

Use of the ATR is governed by guidelines and procedures developed to comply with the institutional policies of both the National Health and Medical Research Council, and The University of Melbourne, as well as privacy legislation, and community and member expectations. These allow all Australian researchers access to the ATR's service on a fair, reasonable and equitable basis, while protecting the interests of twin members.

To facilitate efficient resource management and scheduling, the ATR introduced an Expression of Interest (EOI) procedure in 2005. This procedure has proven very useful not only in allowing the ATR to forward plan for upcoming activities, but also to assist in the development of researcher's ideas prior to their seeking funding. It has also facilitated promising connections between research groups with similar goals, which could ultimately result in a higher quality of output and more efficient use of precious research funds. The ATR provides In Principle Approval for EOIs 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 use of the facility.

Formal application is required by researchers to access the Australian Twin Registry. The Application outlines the study's objectives and context; the full details of all that will be asked and/or required of the participants; the amount of time involved; any follow up that might occur; the details of any possible risks associated with participation, particularly where invasive techniques are concerned and details regarding who to contact with questions in relation to the study. It must include a copy of all activities proposed for use during the study. The Application must also describe any benefits to the twin members, including remuneration or incentive. The

receipt of an Application by the ATR initiates a drafting process around the documentation used to invite the twin members to participate.

The Application is circulated to the Research Facilitation Group (RFG), which is made up of the ATR Director, Deputy Director, Administrative staff, and representatives from **match**, WATCH and WATR.

The Application process and documentation were updated and relaunched in late 2006. This activity increased the clarity of the process and encourages more useful dialogue between the ATR and researchers.

REVIEW

The ATR undertakes responsibility to ensure that each proposed research project is:

- of scientific merit
- of significant value to the proposed area of research
- able to comply with appropriate ethical guidelines
- able to be suitably answered utilising a twin model
- an appropriate use of the ATR facility
- clearly described to allow participants to provide informed consent
- not of an unreasonable burden to study participants

The RFG reserves the right to solicit confidential advice or review from external researchers with expertise in the area of study to inform the RFG regarding any of the points above.

The Application process is intended to be collaborative whereby the ATR actively works with the researcher to improve and refine the proposed study and associated documentation. This collaboration often proves valuable to the researcher. The researcher is expected to resolve any serious issues that have been raised by either the ATR or external reviewers to their respective satisfaction before the ATR's approval for the study is granted. This collaboration is undertaken with the assumption that improvements to any research project with which the ATR is involved benefits not only the researcher but also the ATR and ATR members.

ETHICS

The NHMRC National Statement on Ethical Conduct in Human Research emphasises each *"institution's responsibilities for the quality, safety and ethical acceptability of research that they sponsor or permit to be carried out under their auspices"*. This statement includes those institutions whose *"employees, resources and facilities are involved in research"*. The ATR is therefore invested under these guidelines to ensure the ethical conduct of both its own activities, and the associated activities of research projects for which it recruits.

In 2007, the ATR was awarded University of Melbourne Human Research Ethics Committee approval for the 'Program of Work' supplied to researchers. This Program approval provides ethical auspice for the ATR's activities and enables a mechanism to ensure that all work associated with the ATR is ethically sound. Under this system, researchers are required to obtain HREC approval for their research project utilising their own local institutional HREC, and these approvals are then registered with The University of Melbourne HREC under the ATR's Program of Work.

CURRENT RESEARCH STUDIES

Enabling Grant Goal:
Increase number of studies supported by the ATR to 15 – 20 per year

The ATR has set a goal for increasing the number of studies supported per year to between 15 and 20. This includes: studies that are in the initial stages of planning and development; studies which are involved in active recruitment and; those which have finalised recruitment but may require additional support for follow up and clarification with members.

While the rate of studies supported has been slowly rising, the range, size and sophistication of these studies have increased markedly.

Table 1 shows that as at the end of Year 3, the ATR was actively recruiting for 15 studies, with 2 studies approved and waiting to start recruitment, and 1 study awaiting ethics approval. 2 additional studies were in Full Application phase and 1 was undertaking a protocol change.

The ATR has also increased the support made available to researchers moving from the EOI to Full Application phase. This facilitation has, on a number of occasions, significantly improved the quality of the study for the benefit of all involved.

Table 1: Study Status

Study Status	Number of Studies
Discussion	4
Eoi	11
Full Application	2
APPROVED – ETHICS	1
APPROVED – WAITING TO START	2
ACTIVE – RECRUITING	15
ACTIVE – PROTOCOL CHANGE	1
ACTIVE – ONGOING PROGRAM	13
ACTIVE – DATA ANALYSIS	17
ACTIVE – WRITING UP	4
COMPLETED	48
ON HOLD	4
Total	122



SCIENTIFIC MERIT

Collaboration with researchers applying to the ATR to ensure that projects are of significant scientific merit and are appropriately described to ensure potential participants are able to provide informed consent

RESEARCHER REPORTS

The following Researcher Reports provided by the researchers and associated staff summarise the current activities undertaken by each study, major achievements for this period and future plans. Appendix 1 provides a full listing of all studies by status.

Please note: listed in alphabetical order of surname of Principal Investigator

2003-001-1

Genetic & Environmental Risk Factors in Myopia – A Twin Study

2006-003

Myopia and Personality

Principal Investigator:

Dr Paul Baird

Centre for Eye Research Australia, VIC

The primary aim of the Genes in Myopia (GEM) twin study is to investigate the relative genetic contribution to myopia (short-sightedness) and associated ocular parameters using a classical twin model. The researchers also endeavour to examine the relationships between body stature, personality traits and environmental risk factors and myopia.

The preliminary findings from the current study have provided substantial evidence to support a genetic basis to myopia, with the information of twins now being used to identify gene(s) involved in myopia. The study has addressed limitations coming from previous twin studies by examining both female and male twins, having a wide age selection and providing information on environmental risk factors and ocular parameters associated with myopia. With these data, the researchers have been able to provide very useful insights into environmental and other risk factors associated with myopia.

The researchers have recruited and examined 1224 twins, making this the largest twin study in the world to investigate myopia in adults. The findings from the current study have been published in prestigious eye journals, presented at both national and international conferences and have received a large amount of media interest.

The researchers have shown through the use of genetic (heritability) modelling that up to 85% of the variance (the variability of the data) of myopia can be explained

by genetic factors, which gives the researchers confidence to search for causative myopia genes. Therefore, the researchers are now entering the final phases of the study, which will primarily involve the use of genetic testing (linkage study) to identify gene(s) involved in myopia.

As part of a joint project, the researchers intend to recruit twins reared apart through the ATR to better understand the significance of the environmental component in myopia. This study will be invaluable to identifying both common and unique environmental risk factors that may be playing a role in myopia. The researchers would also like to explore the role of IQ in myopia.

Funding:

Australian Federal Government through the Cooperative Research Centres Program	2003-2010	\$300,000 pa
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Joan and Peter Clemenger Trust	2007/2008	\$50,000
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L. E. W. Carty Trust	2007/2008	\$114,000
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Status: ACTIVE – ONGOING PROGRAM

97-001-3

Morphological and Spectroscopic Study of Monozygotic Twins Discordant for Epilepsy

Principal Investigator:

Professor Sam Berkovic

Epilepsy Research Centre, VIC

The general strategy of this study is to combine the power of high resolution MRI examination with clinical studies in twins to help understand the structural and metabolic basis of epilepsy. The researchers will analyse the differences between MRI brain structure and function between MZ twins discordant for epilepsy and healthy control MZ twins.

The difficulty in disentangling critical aetiological factors in epilepsy relates to the biological variability in people with epilepsy, both genetically and for exposure to acquired factors. By using twins, with the same genetic make up and similar environmental exposure, subtle differences explaining the aetiology of the disease may be apparent that cannot be easily discovered without very large sample sizes in the singleton population.

During this period data analysis was completed for the control (healthy) MZ twins and a manuscript is in preparation. Goals for the following year are to complete and submit a manuscript on the data from the control MZ twins and to identify and scan more MZ twin pairs discordant for epilepsy.

Funding:

NHMRC Program Grant 2006-2010 \$11,361,070

Status: ACTIVE – RECRUITING

98-001

Genetics of Reading Ability

Principal Researcher:

Professor Brian Byrne,

University of New England, NSW

The aims of this study are to identify genetic and environmental influences on children's early development in literacy, language and attention and to also track these influences as they play out across development from age 4 to about 9.

This project is one of only a few that follow the twins longitudinally, starting prior to formal schooling. The amount of data collected on each child, amounting to about 7 hours in total, is unique. The researchers are also collecting DNA with a view to possible future genome-wide scanning in the search for genes impacting on literacy growth. The study is also unique in including samples from four countries (Australia, USA, Norway, and Sweden), spanning three languages.

In the last two years the researchers have conducted analyses of school-age data, and as well as performing univariate analyses of literacy and language levels, have examined developmental trends. Thus the researchers have been able to show both genetic continuity and genetic change during literacy growth, and also demonstrated gene-environment interactions as they play out in different educational cultures (Scandinavia, Australia, and the USA).

As well as continuing to collect data on successive waves of twin recruits, the researchers are applying for funds to follow the US sample until the age of 12. The researchers are also working with a new group in Japan, who have adapted assessment tools for Japanese, and are starting data collection during the 2007 northern summer.

Funding: ARC 1999-2009 \$827,000

NIH 2001-2005 \$580,000 (USD)

Status: ACTIVE – ONGOING PROGRAM

2007-004

Role of genetic and environmental factors in atrial fibrillation

Principal Investigator:

Associate Professor Diane Fatkin

Sr Bernice Research Programme in Inherited

Heart Diseases, Victor Chang Cardiac

Research Institute, NSW

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia and a major cause of morbidity and mortality. Until recently, AF was regarded as a sporadic, non-genetic disorder. However, there is now accumulating evidence that familial aggregation of AF occurs in a substantial proportion of cases. Although very little is known about the role of genetic factors in AF, it is likely that AF in the majority of individuals is a complex multifactorial disorder in which a combination of one or more genetic factors that increase susceptibility to AF and/or acquired "environmental" factors that alter atrial size and/or function are involved. Twins are a useful resource for determining the relative contribution of genetic and environmental factors in the development of AF. The researchers believe that understanding the molecular pathogenesis of AF in twins will facilitate studies of DNA variants that might increase susceptibility to AF in the general population and provide a basis for development of novel drug therapies. Determination of the relative contribution of genetic and environmental factors in twins and other AF populations may also indicate the expected benefits of aggressive modification of underlying conditions, such as hypertension, that can predispose to AF by altering the atrial environment. Given the paucity of current knowledge, the new data generated by this study will provide a significant contribution to the field.

The aims of this study are to:

- collect clinical details and blood samples from a sample of monozygotic (MZ) and dizygotic (DZ) twin pairs in which one or both twins has AF.
- determine the heritability of AF using a sample of MZ and DZ twins.
- identify and characterize disease-susceptibility genetic polymorphisms.

Funding: Pending

Status: Full Application – REVIEW



2007 SCIENTIFIC MERIT

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2006-004

Genetic and environmental factors in invasive cervical cancer: a twin study

Principal Investigator:

Suzanne Garland

Royal Women's Hospital, Melbourne, VIC



United effort: (L-R) 2006 Australian of the Year Professor Ian Frazer with Professor Diane Harper, Michael Quinn and Suzanne Garland

This will be the largest-ever twin study to examine factors related to persistence of Human Papilloma Virus (HPV) infection and development of high grade squamous intraepithelial lesions (HSIL). The twin design is the most appropriate and powerful design to examine the role of environmental and genetic factors simultaneously. HSIL is a relatively rare outcome of HPV and although large numbers of twins are being studied, it is possible that the study may be underpowered for this aim. However, the use of twins reduces the required sample size, and additional twin pairs are being recruited, which will increase the available numbers. Persistence of HPV infection, a necessary prerequisite for HSIL, is the reason for the development of a detailed algorithm to classify twins, which is consistent with international studies. Another Australian study was recently funded to examine hormonal factors in relation to HSIL, using a traditional case-control design; however, the present study is unique in that it addresses both genetic and environmental factors and in particular factors determining persistent infection.

The study has 3 aims:

- to assess whether genetic and environmental factors influence the development of persistent infection with high-risk (HR) HPV genotypes of the cervix
- to assess whether genetic and environmental factors influence further progression to cervical cancer (using HSIL abnormalities as a surrogate) among women infected with HR HPVs

- to assess the negative predictive value of HPV 16 and 18 serology for pre-existing infection by recruiting twins with no history of an abnormal Pap result, nor HPV DNA positivity

At this stage, the project team is liaising with cervical cytology registries and pathology providers, and undertaking development of the questionnaire and database. Recruitment of twins is scheduled to commence in late 2007. Retrieval of Pap smears from Pathology providers for HR HPV DNA testing and serology for HPV will then commence.

Funding:

Cancer Council Victoria	1 year	\$30,000
University of Melbourne	1 year	\$70,000

Status: APPROVED – WAITING TO START

2007-001

Cortical and trabecular bone mass response to 12 month calcium and vitamin D supplementation in monozygotic preadolescent female twins

Principal Investigator:

Dr David Greene

Australian Catholic University, NSW



ATR member Kelsey having a bone density scan of her lower leg. Kelsey and her twin Abbie are participating in the bone mass study

Conflicting evidence surrounds the beneficial effects of calcium supplementation on bone mineral density during childhood and adolescence. No study has used three-dimensional bone imaging, such as peripheral quantitative computerised tomography (pQCT), to assess the effect of calcium supplementation on bone material properties in a well matched cohort of twins. In contrast to previous studies in which unrelated individuals are compared, the study will control for genetic and environmental confounders by determining within-pair differences in

bone material properties in female preadolescent monozygotic twins. It is hypothesised that females randomised to receive calcium and vitamin D supplementation for a period of twelve months will display increased bone material properties at the tibia and distal radius compared to their twin who has been randomly chosen to receive a placebo.



ATR member Abbie having a bone density scan of her wrist. Abbie and her twin Kelsey are participating in the bone mass study

This study has two aims: to determine within-pair differences in trabecular and cortical bone material properties at the distal tibia and radius in a well matched cohort of preadolescent female twins at baseline, six-months, and twelve months after receiving either daily calcium and vitamin D supplementation or a placebo for a period of twelve months, and; to assess the influence of calcium and vitamin D supplementation on trabecular and cortical bone material properties at the distal tibia and radius independent of body size, height, weight, and age using regression analysis.

Plans for the following year include further data collection Jan / Feb and July / Aug 2008, with the aim to submit 6-month data for publication in March 2008.

Funding:
Dean's Initiative Fund
(Health Sci) 2007 \$5000
In kind support for project has been received
from USANA Health Sciences Inc.
Status: ACTIVE – RECRUITING

2003-001

Genetic & Environmental Risk Factors in Age-related Macular Degeneration – A Twin Study

Principal Investigator:
Professor Robyn Guymer
Centre for Eye Research Australia, VIC

Age-related macular degeneration (AMD) is the leading cause of poor vision in Australia. The aim of this study is to better define the heritability of age-related macular degeneration, and to uncover potential new risk factors for the disease.

Ultimately, understanding the genetics of AMD will lead to a better understanding of the pathogenesis of this disease, and hopefully identify areas where treatment can be targeted. Similarly further identification of environmental risk factors will enhance knowledge of the pathogenesis of AMD, and may lead to better public health strategies to reduce the burden of disease.

6 papers have recently been published and several international scientific presentations have been made; further publications are planned.

Funding:
NHMRC project grant 2007 \$50,000
Status: ACTIVE – ONGOING PROGRAM

2007-002

Impact of Folic Acid (FA) on Perinatal Outcome of Twins

Principal Investigator:
Jane Halliday
Murdoch Children's Research Institute, VIC

The aim of this study is to investigate if there is a difference between the perinatal outcomes of twins of mothers who took folic acid during the periconceptional period with twins of mothers who did not take folic acid during this period. Perinatal outcomes include factors such as gestation of pregnancy, birth weight, health and well-being.

Folic acid is the tablet form of the B group vitamin folate, found in foods such as leafy green vegetables, oranges, berries and eggs. Its use has been shown to reduce the number of babies born with neural tube defects, such as spina bifida.

Because of the established benefits of folic acid, and because obtaining sufficient amounts of the vitamin from food sources can be difficult, mandatory fortification of all bread mix flour in Australia and New Zealand is going to be introduced.

Currently not all the outcomes resulting from taking folic acid are well understood, so it is vital to better



2007 SCIENTIFIC MERIT

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understand all the consequences of taking folic acid with mandatory fortification taking place. One argument against mandatory fortification has been that folic acid may increase the rate of twins being born, who may have poor perinatal outcomes that outweigh the benefits of folic acid. The researchers recently conducted a systematic review of previous studies and found that there was no convincing evidence of this. The current study seeks to address the impact of folic acid on twin outcomes by asking mothers of twins about their folic acid intake before and during pregnancy, which the researchers will do through a short telephone questionnaire.

The researchers are in the final stages of obtaining ethics approval from both the Department of Human Services and the Royal Children's Hospital, and are looking forward to recruitment of participants during late 2007.

The study is due for completion by mid 2008. Publication of the results from this study will be important for informing policy and monitoring outcomes related to the mandatory fortification of foods with folic acid in Australia.

Funding:
Murdoch Childrens Research Institute 2007-2008 \$31,000
Status: Ethics

2002-004-3

Solving the Jigsaw! Understanding biological and environmental effects on ADHD through discordant monozygotic twins

Principal Investigator:
Professor David Hay
Curtin University of Technology, WA

The recent Child and Adolescent component of the National Mental Health Survey identified Attention Deficit Hyperactivity Disorder (ADHD) as the most common behavioural problem in Australian children. Since 1991 the Australian Twin ADHD Project (ATAP) has developed as one of the world's largest research study of genetics and ADHD, and in 2001 the researchers published the first text on this topic.

In this study the researchers turn the focus onto environmental influences with the question "Why can one identical twin have ADHD, while the other twin has no difficulties?" Using the unique resources of the Australian Twin Registry and the WA Twin Child Health Study, the researchers are working across the country to find over 100 identical twin pairs who are very different with regards to ADHD. In this way, each ADHD affected twin has an unaffected 'control twin', offering a powerful means for comparing the two. Such a study is really only possible in Australia, as no other country has a database on ADHD as extensive as ATAP. Over 4000 sets of twins and their siblings have been screened in order to find 100 discordant pairs. This huge resource is being used in many other ways such as developing new measures of ADHD and other behavioural problems which often co-occur, and new methods of genetic analyses to understand the overlap between behavioural disorders.

The questions the researchers want to consider include the following:

- Twins have a more difficult time before and at birth - to what extent do these problems contribute to behavioural differences between the twins?
- Is it that one twin grows out of their ADHD but the other does not? If so, what distinguishes these children?
- What is it like growing up with a twin who has ADHD when you have no difficulties yourself?
- When one twin has ADHD symptoms, is the family more likely to seek help if there are other problems?

Achievements this year include collection and data entry of information from 2,790 families, ten published papers, one paper submitted, and one paper in preparation. Twenty-one conference presentations were also made.

Goals for next year are to continue data analysis and writing up further research papers.

Funding:
NHMRC 2003-2005 \$595,862
NIH 2005-2009 \$2.4million (USD)
Status: ACTIVE – RECRUITING

91-002

Prevention of coronary disease – A genetic approach “The Victorian Family Heart Study”

91-002-2

The Family Study of Heart Size

91-002-3

The Prevention of Coronary Disease – A Genetic Approach: The Androgen Receptor and Female Androgenetic Alopecia

Principal Researcher:
Professor Stephen Harrap
University of Melbourne

The Victorian Family Heart Study aims to identify the genetic contributors to risk factors for coronary heart disease.

It is one of the few studies internationally that combines population-based family studies in which there is enrichment with families containing twins. This provides greater opportunity to define and quantify the genetic and environmental components of coronary risk factors. This will allow us to not only discover genetic mechanisms, but also place them in a community context.

The study has made world first discoveries in the genetics of high blood pressure and male pattern baldness and contributed significantly to the genetics of cholesterol and height. This has resulted in publications in leading international journals and presentations around the world. The project has also supported a number of high achieving research students.

The researchers plan to continue to search for the genetic clues to coronary risk that will lead to new physiological studies of the mechanisms by which such genes operate so that they might devise new means of prevention and treatment. Supporting this operation is the ongoing critical development of statistical models for the sophisticated and complex models that allow us to derive the right answers from the data.

Funding:

Victorian Health	'92	\$150,000
Promotion Foundation	'93	\$159,000
	'94	\$168,540
	'95	\$170,000
	'96	\$170,000

NHMRC	'96	\$53,340
	'97	\$36,271
	'98	\$36,271
Clive & Vera Ramaciotti Foundation	'96	\$30,000
NHMRC	'98	\$59,310
	'99	\$62,269
NHF	'00	\$45,000
	'01	\$45,000
NHF	'01	\$32,400
NHMRC	'00	\$128,544
	'01	\$132,243
	'02	\$135,941
NHMRC	'02	\$155,000
	'03	\$160,000
	'04	\$140,000
NHMRC	'03	\$120,000
	'04	\$120,000
	'05	\$120,000
ARC	'04	\$200,000
	'05	\$190,000
	'06	\$180,000
NHF	'05	\$60,000
	'06	\$60,000
Status: ACTIVE – DATA ANALYSIS		

2002-004-4

Two Approaches to the Molecular Genetic Analysis of ADHD Subtypes in Australian Twins

Principal Investigator:
Professor David Hay
Curtin University of Technology, WA

The aims of this study are twofold

- to investigate the genetic components of an Attention Deficit Hyperactivity Disorder (ADHD) subtype and Reading Disorder (RD) separately and in combined form, to determine whether candidate genes of ADHD and RD comorbidity are the same or if each disorder has its own genes and;
- to confirm if the Latent Class Analysis (LCA) approach represented by ADHD/RD categorical data will be successful in genotyping analyses studies.

The genetics of ADHD/RD comorbidity are still not well understood. This study found a genetic pattern for



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ADHD/RD comorbidity based on finding genes such as COMT, SNAP-25, and KIAA0319 acted differentially on RD alone, ADHD alone, and comorbid ADHD/RD latent classes.

The study highlighted that the use of Latent Class Analysis (LCA) approach is more appropriate than DSM-IV for ADHD/RD genotyping analysis, as each cluster of ADHD/RD latent class was biologically similar, to the extent that these ADHD/RD latent classes represented more aetiologically pure genetic forms of disorders. Plans are underway to publish the study findings.

Funding:
NHMRC 2004-2006 \$12,500
Status: **ACTIVE – DATA ANALYSIS**

2002-004-5

Family and Sibling Relationships When Twins Are Discordant for Attention Deficit Hyperactivity Disorder (ADHD)

Principal Investigator:
Professor David Hay
Curtin University of Technology, WA

Attention Deficit Hyperactivity Disorder (ADHD) is a common childhood disorder which affects an estimated 6% of Australian children and adolescents and occurs more often in twins than in singletons. There are three subtypes of ADHD including the predominantly inattentive type (ADHD-I) and the combined type (ADHD-C). Despite the extensive research studying twins with ADHD, few studies have focused on the psychosocial consequences of having a twin with the disorder. Non-twin research that investigates the impact of ADHD on sibling relationships suggests that siblings of ADHD children experience considerable disruption and have increased levels of conflict and caretaking responsibility in their relationship with their ADHD brother or sister (Kendall, 1999). The close bond that twins often share may result in a greater impact on a co-twin compared to a sibling of a different age.

The primary aim of this study is to investigate the positive and negative effects that non-ADHD co-twins experience from their twin relationship with an ADHD-affected twin.

To date all data have been collected, scored, and entered into a computer database. Preliminary results have been presented at Eunethydis Conference, Bruges 2006; Twin Studies Conference, Gent 2007 and; the ISRCAP Conference, London 2007. The following year will see completion of data analysis and final write-up of a PhD thesis.

Funding:
Curtin University of Technology Term of PhD \$3000
Status: **ACTIVE – DATA ANALYSIS**

2004-002

Investigations of ADHD: Magnetic Resonance Imaging

Principal Investigator:
Professor David Hay
Curtin University of Technology, WA

MZ twins discordant for ADHD are rare and there is much interest in whether there are differences between such twins in brain structure. This study sought to determine the feasibility of pooling imaging data from four sites (St Louis, Vermont, Amsterdam and Australia).

This study has the potential to link the world's four largest ADHD informative cohorts for twins and siblings, allowing the understanding of more about the environmental factors that may influence the brain in ADHD.

Significant achievements include the completion of the Australian phase of data collection and the identification of several key issues – the need for good obstetric data (in twins discordant for Inattentive ADHD, there was a close association with birth difficulties, especially lack of oxygen at birth) and problems in pooling data cross sites despite the use of identical calibration models.

Data are now with collaborators in St Louis for neuro-imaging.

Funding:
NIMH 2002-4 \$175,000 *

*Note this funding was spread across four sites
Status: **ACTIVE – ONGOING PROGRAM**

2002-004-6

Developmental correlates of reactive and proactive aggression

Principal Investigator:

Professor David Hay

Curtin University of Technology, WA

The role of aggression within disruptive behaviour disorders has not been well understood. Investigation of mechanisms underlying the emergence of different forms of aggression (as well as the relationship between these mechanisms and non-aggressive disruptive behaviours) aims to assist researchers and clinicians to identify developmental markers of chronic and life-course persistent antisocial behaviour and at the same time improve diagnostic frameworks designed to guide intervention.

The study aims to assess genetic influences on neuropsychological correlates of reactive and proactive aggression across development. More broadly, the study hopes to contribute to research concerning (putative) differential mechanisms underpinning different forms of aggressive behaviour and non-aggressive disruptive behaviours (including ADHD symptomatology).

In the last two years (2005-2007) a number of neuropsychological tasks have been programmed in a format that allows them to be delivered over the internet. A task interface has been developed and a sophisticated database set up to store information contributed by families online. The significance of this for genetic research is that obtaining the necessary sample size for this kind of research has previously been prohibitive. The study has signed up over 650 families from across Australia who are now able to contribute to the study online. Over a third of these families have already completed the study which includes the neuropsychological tasks along with a parent-rated behaviour questionnaire. Families continue to sign up and the study will be extended due to the positive response.

Once the study is taken offline at the end of September 2007, data analysis will commence. This will include multivariate genetic analyses of reactive and proactive aggression and ADHD symptomatology. It will also include an assessment of how the genetic architecture

of these constructs changes over development. Finally, a longitudinal analysis will aim to shed light on the developmental relationship between aggression and ADHD. Early in 2008 these results will be written up in a PhD thesis and of papers will be published. In addition, ATR families who have requested feedback of the results will receive a summary of the results of the study.

Funding:

Curtin University
of Technology

Term of PhD

Note: See
2004-002

Status: ACTIVE – RECRUITING

2002-004

Genetic comparison of two measures of Attention Deficit Hyperactivity Disorder (ADHD)

Principal Investigator:

Professor David Hay

Curtin University of Technology, WA

The SWAN (Strengths and Weaknesses of Attention) Scale is the first measure of ADHD which does not focus simply on negative symptoms of attentional problems but allows for the child to do better than average. This has created great interest in intervention studies and also for those molecular genetic studies that require extremely concordant and discordant pairs of twins or siblings.

The aim of this study was to determine the heritability of the SWAN Scale and its bivariate heritability with conventional measures of ADHD according to the usual diagnostic criteria.

This study formed a pilot for the much larger study "Solving the Jigsaw" (ATR 2002-004-3) and was the basis for revising the questionnaire for that study. The 2007 paper in *Biological Psychiatry* was based to a significant extent on data from this project.

Funding:

Discretionary funding
by Curtin University of Technology

2002-2003

\$20,000

Status: ACTIVE – DATA ANALYSIS



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2005-002

Molecular Genetics of Inattention in Australia

Principal Investigator:
Professor David Hay
Curtin University of Technology, WA

There are several existing genetic linkage studies based on extended families or affected sib-pairs with ADHD and at least another 15 studies looking at the associations of ADHD with polymorphisms of candidate genes. A search of the National Institutes of Health (NIH) Commons CRISP website indicates 4 NIH-funded extramural linkage studies of ADHD including a Finnish study, US and European consortium studies and a Missouri study.

The study specifically aims to investigate affected and discordant sib-pairs from twin families (N=300) identified as having severe attention problems. There has been probably more success in finding candidate genes for ADHD than for any other behavioural disorder. But the problem remains as to what should be the phenotype for molecular genetic analysis. Simply taking those who meet the criteria for "ADHD" probably involves heterogeneity of aetiology. The researcher's US collaborator, Professor Richard Todd in St Louis, developed the concept of using the statistical technique of latent class analysis to identify more homogeneous groupings within ADHD and in a series of papers the researchers have shown these classes apply to Australian families and are genetically distinct. One class the researchers have identified is that of severe Inattention with few symptoms of Hyperactivity and Impulsivity.

The immediate goals of this proposal are to complete a genome-wide linkage scan to identify chromosomal regions involved in severe inattention problems as defined by a quantitative trait and by latent class analysis, and to test for known candidate gene effects in this population-based sample. The long-term goal is to identify genes contributing to inattentive ADHD and other related disorders.

To date all ethics approval has been obtained, interviewers have completed the training program and recruitment has been commenced.

92 families so far have been recruited (81 of these were eligible for the study). Within the 81 families there were 41 children aged 7-11 (not eligible for interview) and 218 children aged 12-29 (eligible to be interviewed). Out of the 218 children eligible for interview, 178 have now been interviewed. Out of the 81 mothers, 53 have been interviewed. The goal of the following year is to increase recruitment to achieve the goal of 300 families.

Funding:
NIH 2005-2010 \$2,542,254 (USD)
Status: ACTIVE – RECRUITING

98-008

Australian Breast Cancer Twin Family Study

Principal Researcher:
Professor John Hopper
University of Melbourne, VIC

This is a study of the genetic epidemiology of breast cancer, and includes a sample of 60 twin pairs where one or both have had breast cancer, recruited through the ATR.

This work contributes to the world-wide research into the genetic and familial aspects of breast cancer, the most common cancer among Western women.

The broader study has made many achievements, especially in terms of characterising the roles of known genes, BRCA1, BRCA2 and ATM in terms of breast cancer risk.

Through continued funding from NIH (USA) for 2006-10, the researchers will be following up all participants (including the twin pairs) about 10 years after their recruitment to the study.

Funding:
NIH 1995-2010 \$100,000 (USD)
Status: ACTIVE – RECRUITING

94-005

A twin study of mammographic breast density and the risk of breast cancer

94-005-2

Genetic and Environmental determinants of mammographic density: A twins and sisters study

Principal Researcher:
Professor John Hopper
University of Melbourne, VIC

The aim of this project is to study the genetic and environmental determinants of mammographic density, a strong and heritable risk factor for breast cancer.

Mammographic density, the area of bright white on a woman's mammogram, is increasingly becoming recognised as a strong risk factor for breast cancer. Understanding why this is so may lead to major improvements in identifying other risk factors for breast cancer, and for developing interventions to prevent the disease. This twin study demonstrated, in collaboration with Canadian colleagues, that the reason why women of the same age differ so widely in mammographic density may be due to genetic factors. The researchers are using the twins of this study, together with their sisters and sister pairs from other studies, to try to find those genes.

The researchers have now recruited more than 2,000 Australian twins and sisters into the study and digitised more than 10,000 mammograms. The researchers have conducted a study of candidate genes that has already resulted in one publication and have written a grant to the National Breast Cancer Foundation (NBCF) to conduct more gene studies. With Canadian colleagues, the researchers have been awarded a large NIH (USA) grant to conduct a genome-wide scan using DZ and sister pairs to try to find new mammographic density genes. The researchers have also been awarded a grant in the name of Prof Mitch Dowsett (London) from the Da Costa Foundation to conduct a twin study of hormone levels using blood samples from the twins. Preliminary analyses have shown that familial factors explain a large proportion of variance in post-menopausal women, and the researchers intend to continue this study.

Activities planned for the following year include finalising recruitment of the current study, isolating DNA, conducting candidate gene studies, sending DNA to Toronto for genome-wide scans and statistical analyses.

Funding:

Australia Fellowship, till 2012 >\$1 million
VBCRC, NIH

Status: **ACTIVE – RECRUITING**

2006-001

Cannabis and Other Illicit Drug Use: A Twin Study

Principal Researcher:
Dr Michael Lynskey
Washington University, USA

There is the widespread use of cannabis, increasing recognition of the potential health effects of this drug and a growing recognition of cannabis dependence as a distinct clinical entity. This project will conduct a genetically informative research study of the assessment of cannabis use disorders, stages of development in and escalation of cannabis and the development of cannabis use disorders, and the mental health correlates of cannabis use, including escalation to the use of other drugs.

The project will interview a sample of 6,600 young adult Australian twins using a structured interview assessing lifetime history of cannabis and other drug use and use disorders, and related aspects of substance use and mental health. Specific aims are:

- to examine the links (genetic or environmental) between early cannabis use and escalation both to the use of other drugs (cocaine, amphetamines, heroin and other opioids, sedatives, hallucinogens, ecstasy) and to drug abuse/dependence.
- to assess the psychometric properties of an assessment of cannabis use disorders within the context of a genetically informative research design; and to examine the extent to which early onset cannabis use may be differentially associated with specific components of abuse/dependence via genetic versus environmental mechanisms.
- to examine whether apparent links between early cannabis use and subsequent illicit drug use and abuse/dependence can be explained by hypothesized social factors, including exposure opportunity and the nature of peer affiliations at the time of initiation to cannabis use (reported retrospectively).



SCIENTIFIC MERIT

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- to explore the links (genetic or environmental) between cannabis use and dependence and other measures of common mental health problems (major depressive disorder, persistent suicidal ideation, suicide attempt) and, in particular, to examine the extent to which continued or escalating cannabis use may exacerbate pre-existing mental health problems.

There have been a number of significant achievements for this project in the past 12 months. Plans for data collection (e.g., interview schedule etc) have been finalized, ethics and other approvals received and data collection has commenced. To date, a total of 657 interviews have been completed with members of this sample. The researchers hope to continue recruitment and interviewing of this sample over the next 12 months.

Funding:

NIDA* 2005 – 2010 \$1,018,714(USD)

*U.S. National Institute of Drug Abuse

Status: ACTIVE – RECRUITING

2007-003

The heritability of rational (analytical) versus experiential (intuitive) reasoning: A pilot study

Principal Investigator:
Dr Anthony Marks
School of Behavioural, Cognitive and Social Sciences, University of New England, NSW

Many research initiatives into problem behaviours invoke the dual-process perspective of decision-making. The dual-process perspective suggests that human behaviour is controlled by two distinct information processing systems: (1) a rational system that is conscious, effortful, logic-based, and largely affect free, and (2) an experiential system that is predominantly preconscious, automatic, and tied to intuition and affect.

Individuals are known to differ in terms of their relative preferences for these two systems. Moreover, research has shown that an individual's preferred mode of cognition is associated with susceptibility to judgment biases. Individuals with a preference for rational thinking tend to be less susceptible to cognitive

judgment biases and fallacies, whereas those with a preference for experiential thinking are more prone to such biases and fallacies.

In association with the Australian Twin Registry the proposed study will recruit pairs of monozygotic and same-sex dizygotic twins in order to investigate:

- a) the extent to which preferred mode of cognition is heritable;
- b) the extent to which susceptibility to judgment biases is heritable;
- c) how much genetic overlap is present across the different judgment biases examined in the study. Do there appear to be different genes operating for different biases, or do the same genes appear to be implicated in multiple biases?
- d) the extent to which the genes responsible for susceptibility to judgment biases overlap with those responsible for individual differences in preference for rational and experiential cognition and also working memory capacity.

The working hypothesis is that genetic differences responsible for preferred mode of cognition and working memory capacity will also underlie susceptibility to judgement biases.

The biased decision-making stemming from the preference for experiential rather than rational cognition is also implicated in problematic behaviour such as smoking, drug and alcohol abuse and certain forms of aggression. It is therefore important to learn to what extent individual preference for rational versus experiential cognition is inherited and, if so, whether it is linked genetically to susceptibility to judgment biases and fallacies.

This year development and testing of online series of assessments and questionnaires was completed. The project is currently awaiting HREC approval and recruitment is expected to commence August 2007 with the study expected to be completed January 2008.

Funding:

UNE Research ongoing \$7,500

Incentive Funds

Status: Ethics

2001-005

Twin study of ophthalmic screening parameters

2006-006

Genetic and environmental contributions to retinal microvascular signs in Australian twins.

Principal Researcher:
Professor David Mackey and Professor Tien Wong
Royal Victorian Eye & Ear Hospital

Glaucoma is the second leading cause of irreversible blindness in Australia. There is a strong genetic component to glaucoma and twin studies allow us to explore the genetic nature of those components of the eye that are implicated in this condition. By identifying the genes involved in the normal variation of glaucoma screening parameters (intraocular pressure, optic disc size and corneal thickness), the researchers hope to identify genes that, with a severe mutation, may cause glaucoma. The major impact of new glaucoma gene discoveries will be better diagnosis and treatment of glaucoma. The researchers are also investigating numerous environmental factors that have been associated with glaucoma and related ocular measurement. Retinal blood vessel caliber is a novel marker of many eye and systemic diseases. Research indicates retinal vascular caliber changes (e.g., retinal arteriolar narrowing and venular dilation) are related to risk of eye diseases (diabetic retinopathy, glaucoma) and systemic vascular disease (stroke, heart disease, cardiovascular mortality). These studies suggest that subtle changes in retinal vascular caliber, as a sub clinical marker of microvascular disease, may allow prediction of important retinal and systemic diseases.

This study will allow the researchers to address the key question of whether retinal vascular diameter is genetically determined and the strength of the genetic risk in the population. This will provide further insights into the pathogenesis of the complex ocular and systemic diseases. The study aims to expand the research into the genetics of glaucoma by studying the heritability of specific eye measurements used in diagnosing glaucoma. In addition, changes in retinal caliber (e.g., narrowed diameters) have been linked to

glaucoma, diabetic retinopathy as well as stroke, and heart disease, independent of traditional risk factors. In collaboration with Dr Tien Wong and Dr Cong Sung the researchers aim to determine the heritability of retinal vascular diameters as part of the optic disc photographic analysis.

To date the researchers have examined over 1,000 pairs of twins as part of a study into glaucoma screening parameters. This has included celebrity Australian twin singers Jessica and Lisa Origliasso from *The Veronicas* and Melbourne based Ophthalmology Professor Gerard Crock and his twin brother Henry, both of whom have widely publicised the Twins Eye Study. The launch of the www.twinseyestudy.com website on May 1st 2006 was a milestone for the research group. The website presents information at different levels for participants and enables understanding of the research at varied levels.

During the following year the researchers plan to complete all data collection. Many Tasmanian twins have not completed UV fluorescence photography, used to detect conjunctival sun damage. Preliminary work indicates a large difference in ultraconjunctival damage in the Queensland twins compared to those who reside in Victoria/Tasmania and this reflects the variation in ultra-violet (UV) light exposure. The researchers will continue data collection, update twins with zygosity results and prepare a second newsletter with findings of the study.

Funding:

Clifford Craig Medical Research Trust Foundation for Children	2007-2008	\$50,537
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National Eye Institute	2007-2009	2007 \$67,792 2008 \$58,600 2009 \$60,067
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NHMRC	2005-2007	2005 \$203,975 2006 \$234,425 2007 \$239,875
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Ophthalmic Research Institute Australia	2006	\$40,000
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Status: ACTIVE – RECRUITING



SCIENTIFIC MERIT

Collaboration with researchers applying to the ATR to ensure that projects are of significant scientific merit and are appropriately described to ensure potential participants are able to provide informed consent

93-011

Longitudinal Study of Melanocytic Naevi in Twins (Mole Development in Pubescent Twins)

Principal Investigator:
Professor Nick Martin
Queensland Institute of Medical Research, QLD

The aim of this project is to carry out molecular genetic analysis of DNA samples from twins, siblings and parents to identify major genes affecting moliness, pigmentation and other risk factors for melanoma. A further aim is to examine genetic variants influencing several behavioural traits: personality, health and wellbeing, laterality, olfactory function and taste perception. Finding genes that predispose individuals to multiple melanocytic naevi will be informative for melanoma research. The following year will see a continuation of recruitment and testing of the twins.

Funding:		
NHMRC	1995 – 1997	\$254,851
NHMRC	1998 – 2000	\$854,151
NHMRC	2003 – 2005	\$637,000
NHMRC	2006 – 2008	\$627,975
Status: ACTIVE – ONGOING PROGRAM		

95-004

Persistence and change in drinking habits: A twin-family study

Principal Investigator:
Professor Nick Martin
Queensland Institute Of Medical Research, QLD

Data collection for this study (structured diagnostic psychiatric interviews conducted with 6,273 twins) was completed in August 2003. This was the largest twin study of alcohol use/misuse and psychopathology, with a particular focus on women, to be conducted at the time. Data gathered in this study continue to be an important resource for alcohol researchers.

The aims of the study were to examine the role of:

- genetic factors in the development of alcohol use, abuse and dependence
- environmental factors and
- comorbidity (depression, anxiety, eating disorders, cannabis use).

Publications continue to arise from the data.

Funding:		
NIH	1995 – 2000	\$1,298,000 (USD)
Status: ACTIVE – DATA ANALYSIS		

2003-002

The Genetics of Borderline Personality Disorder

Principal Investigator:
Professor Nick Martin
Queensland Institute of Medical Research, QLD

The aim of this project was to initiate a twin study of the genetics of Borderline Personality Disorder (BPD), as well as of the personality dimensions that underlie the symptoms of this disorder; to provide data regarding the prevalence of features of BPD in a community sample; to conduct genetic analyses of the features of BPD as assessed by the Personality Assessment Inventory-Borderline features (PAI-BOR) scale and; to conduct multivariate genetic analyses to determine the extent to which the NEO-PIR assesses the same dimensions of genetic variation as do the PAI-BOR items.

Targeted participants included male and female Australian twins born between 1972 and 1985 and voluntarily registered on the ATR. Due to the insufficient numbers of twin pairs agreeing to participate in this research the study has now been abandoned.

Status: Abandoned

2001-004

The Genetics of Vulnerability to Nicotine Addiction

Principal Investigator:

Professor Nick Martin

Queensland Institute of Medical Research, QLD

There has been very little research designed specifically to identify genes that contribute to risk of addiction to nicotine in humans. This project adds to knowledge in human research of nicotine dependence.

This project aims specifically to identify genes that contribute to risk of addiction to nicotine in humans. The aim is to identify specific chromosomal locations that have at least a moderate effect on risk of nicotine to addiction. This is done by collecting phenotypic information from twins, siblings, spouses and parents using a structured interview and a self-report questionnaire, and genotypic information via blood/buccal samples.

Data collection (via telephone interview and self-report questionnaire) for this project was completed at the end of 2005. In total 3378 interviews were completed and 3038 blood/buccal samples collected. Cleaning of the interview data concluded in April 2006.

All blood samples collected for this project have subsequently had a DNA sample extracted, and standardised to a 50ng/ul working concentration.

Replacement aliquots for those samples which did not successfully transform at Rutgers (N= 317) have been prepared and were shipped to the Washington University laboratory in January this year.

To date, three batches of DNA samples have been sent to AGRF for 400 marker genome scans (total of 1320 samples). Samples were selected by Dr Madden based on affectedness of the families. Results of the genome scans have been received and are being analysed by Dr Madden and her staff at Washington University. A fourth batch of samples (approx n=400) is planned for shipment should funds become available. A grant application for a continuation has been submitted to the NIH-NIDA.

Red Blood Cell fractions for a selection of participants who reported high alcohol intake on their questionnaires will be shipped to Dr John Whitfield's laboratory in Sydney in late 2006 for screening of Pb levels.

Biochemical screening of red blood cells is continuing at the laboratories within RPA in Sydney under the direction of Dr John Whitfield with data expected to become available at the end of August 2007.

Funding:

NIH 2000 – 2005 \$1,928,827 (USD)

Status: ACTIVE – DATA ANALYSIS

2003-003-1

Molecular Epidemiology of Alcoholism 1: Candidate Gene (IRPG 1)

Principal Investigator:

Professor Nick Martin

Queensland Institute of Medical Research, QLD

Alcoholism is a major public health problem and is associated with increased risk of cancer, cardiovascular disease, liver disease, and impaired immune function. In contrast to the large number of gene-mapping studies focused on chronic disease phenotypes such as diabetes or hypertension, and considering the high economic and health-related costs of alcohol misuse, there is remarkably little research activity focused on mapping genes that contribute to alcohol misuse and dependence. This project expands current knowledge in the field.

The aim of this project is to locate genes which make substantial contributions to variation in susceptibility to alcohol dependence and hazardous alcohol consumption.

Phenotypic and blood collection is now complete and the phenotypic data are currently being cleaned in preparation for data analysis which will proceed during the next 12 months.

Funding:

NIH 2001 – 2006 \$2,078,478 (USD)

Status: ACTIVE – DATA ANALYSIS



SCIENTIFIC MERIT

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2003-003-2

Variations in the effects of alcohol on liver function (IRPG5)

Principal Investigator:
Professor Nick Martin
Queensland Institute of Medical Research, QLD

The overall aim of this work is to identify factors which affect the degree of liver function test abnormality caused by hazardous alcohol use.

Various family, adoption and twin studies have shown that alcoholism has a genetic component. Preliminary studies have produced strong evidence of major genetic influences on alcohol dependence in Australian men and women. The researchers have also shown that those less affected by alcohol, and slower metabolisers of alcohol, are at greater risk of alcohol dependence. Most reliably measured variance in ethanol metabolism is genetically determined, but known variants in ADH2 and ADH3 account for only a small proportion of variance in metabolism, or in consumption and problems. Multivariate linkage analysis, which is still in progress, suggests that around half of the reliable variance in alcohol metabolism is due to variants in the ADH region. All these findings point to undiscovered variation in the ADH region which has a major influence on alcohol metabolism, consumption, problems and dependence. Liver disease is a common but not universal consequence of alcohol abuse or dependence. It would be clinically and scientifically useful to determine the causes of variation in susceptibility between individual drinkers.

Preliminary analysis has confirmed the initial hypothesis that variation in Body Mass Index (BMI) and biochemical characteristics related to metabolic syndrome and iron status affects the probability of abnormal liver function tests in at-risk drinkers, and the sensitivity of at least some biological markers in detecting hazardous alcohol use. Differences in results have been shown between men and women. This will allow better interpretation of clinical tests results for these markers.

The researchers plan to continue with:

- Testing candidate genes in the at-risk-drinking group;
- Making use of genome-wide association SNP marker data, in conjunction with linkage marker data, from the entire sample to define loci affecting liver function

in the general population, and those affecting the phenotypes (e.g. BMI, triglycerides, ferritin) which in turn affect GGT and ALT in at-risk drinkers and;

- Investigating a pooling design for genome-wide assessment of loci affecting liver function tests in the at-risk-drinking group

Funding:
NIH 2003 – 2008 \$2,094,038
Status: ACTIVE – DATA ANALYSIS

2003-003-3

Molecular Epidemiology of Alcoholism 3: EDAC Families (IRPG3)

Principal Investigator:
Professor Nick Martin
Queensland Institute of Medical Research, QLD

Alcoholism is a major public health problem and is associated with increased risk of cancer, cardiovascular disease, liver disease, and impaired immune function. In contrast to the large number of gene-mapping studies focused on chronic disease phenotypes such as diabetes or hypertension, and considering the high economic and health-related costs of alcohol misuse, there is remarkably little research activity focused on mapping genes that contribute to alcohol misuse and dependence. This project expands current knowledge in the field.

This project uses combined candidate gene association approach to map genes contributing to heavy drinking and alcohol dependence (AlcD) risk. Because of the strong phenotypic and genetic correlations between alcohol and tobacco dependence the current project also emphasizes joint analysis of alcohol and tobacco dependence phenotypes, to map genes contributing jointly to heavy drinking and tobacco dependence.

Data collection (diagnostic telephone interviews and blood/buccal samples) has now been completed. Data cleaning and molecular work are ongoing. The aim for the following year is to continue data cleaning in preparation for writing papers.

Funding:
NIH 2001 – 2006 \$1,745,359 (USD)
Status: ACTIVE – DATA ANALYSIS

2002-002

A Study of the Potential Causes of Psychosis in a Twin Sample

Principal Investigator:

Professor Bryan Mowry

Queensland Centre for Mental Health Research, QLD

The cause of psychotic disorders is unknown, but there is good evidence that both genes and environment play a role. If genes and other non-genetic factors related to psychosis could be found, then it may be possible to find better treatments that correct the basic causes of the illness and identify factors that protect against the illness. This study will help to provide insight into the inter-relationships of factors that may be involved in causing psychotic disorders.

The goal of this project is to collect a large sample of twin pairs which have at least one member with a psychotic disorder and a sample of control twins where both members are unaffected, in order to investigate the role of genetic and non-genetic risk factors, and behavioural markers reportedly associated with psychotic disorders.

109 twin pairs (218 individuals) have been recruited: 28 dizygotic pairs and 29 monozygotic pairs for which one (discordant) or both twins (concordant) have experienced psychosis and 52 control twin pairs for which neither have experienced psychosis.

The researchers found evidence of altered prefrontal-thalamic circuitry in schizophrenia using an optimised diffusion MRI study (published in *Neuroimage*, 2006). Using twin data, the researchers replicated effects of sex and genotype on gene expression in human lymphoblastoid cell lines (published in *Human Molecular Genetics*, 2007). Expression profiling in monozygotic twins discordant for bipolar disorder identified dysregulation of the WNT signalling pathway (in press, *Molecular Psychiatry* 2007).

In addition to ATR recruitment, the researchers have promoted the study primarily to recruit potential subjects from clinical networks (hospital, clinics in both public and private sectors) and support groups such as Schizophrenia Fellowship. The study has been advertised

using newspaper advertisements, brochures, letters of initial approach, posters around hospitals and community service centres and both formal and informal presentations to mental health workers. The researchers have also contacted private psychiatrists across the Eastern seaboard of Australia via the Royal Australian and New Zealand College of Psychiatrists (FRANZP) and promoted the study at the Twins+ Festival in Canberra in March 2006.

Recruitment and assessment of affected twin pairs will continue. 15 DZ and 15 MZ control pairs will undergo MRI scanning tailored towards constructing detailed maps of structural and functional connectivity in the brain. The control pairs will enable a normative study of genetic influences on the brain's structural and functional connectivity.

Funding:

Stanley Foundation	2001-2003	\$100,000
NHMRC	2003-2006	\$457,500
Ian Potter Foundation	2007	\$50,000

Status: ACTIVE – ONGOING PROGRAM

99-001

Understanding Twins in Situations of Comparison and Competition

Principal Investigator:

Professor Patricia Noller

The University Of Queensland, QLD

The purpose of this work was to explore reactions to competition and comparison in the relationships of adolescent siblings, including twins.

The most interesting aspect of these findings is the dynamic that develops between the sibling and twin pairs. The older sibling, even in twins, seems to have more power in the relationship, whereas the younger sibling is continually working to preserve their relationship with the older one. This dynamic can be seen in the affective reactions, with the younger siblings showing empathy towards the older sibling when they outperform them, and older siblings having



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greater difficulty being beaten by their younger sibling. Younger siblings also played down their success when they outperformed their older sibling and were generally more aware of their older sibling's self-evaluation needs. Older siblings also were more likely to report that they would continue their favoured activities, without any concern for the impact on their twin or sibling. Younger siblings were not comfortable continuing activities where they performed better than their sibling or twin. Thus both members of the dyad seem to be participating in this dynamic, with the older being allowed more power and the younger ceding activities to the older one and engaging in behaviours that protect their sibling's self-evaluation needs.

Though this project has completed data collection and analysis, presentations of the work continue; presented paper at the Association for Cognitive and Behaviour Therapy in Chicago, November, 2006; presented paper at Sydney Symposium on social psychology in March, 2007; plans to present paper at Conference of the Australian Multiple Birth Association in Newcastle in November with Anita Blakeley-Smith.

Funding: ARC 1999-2001 \$108,000
Status: **COMPLETED**

2000-002

Genetically Driven Constructs of Temperament: Assessing Variation in Self-report Scales

Principal Investigator:
Professor Gordon Parker
Prince of Wales Hospital, NSW

The extent to which temperament and personality is shaped by genes is a field of research that is still poorly understood.

This project aims to obtain information on heredity for a number of temperament and personality measures.

Status: **ACTIVE – WRITING UP**

2002-004-2

Monozygotic Twins Discordant for Developmental Coordination Disorder and Attention Deficit Hyperactivity Disorder: An Integrated Approach to the Bio-Psycho-Social Correlates

Principal Investigator:
Research Associate Jillian Pearsall-Jones
Curtin University of Technology, WA

This project assists in elucidating the links and differences between Attention Deficit Hyperactivity Disorder (ADHD) and Developmental Coordination Disorder (DCD), comorbid conditions, and their aetiologies. The study also looked at management and treatment implications for both conditions.

The specific aims of the study are to examine the:

- aetiology of ADHD and DCD based on questionnaire data
- aetiology and relationship between of ADHD and DCD based on face-to-face interviews
- relationship between ADHD, DCD and IQ
- ADHD and DCD and comorbid conditions
- qualitative effects on the family of MZ pairs discordant for ADHD and DCD

Face-to-face assessments of 16 sets of twins in New South Wales, Western Australia, Victoria, Queensland, the Northern Territory and South Australia have now been completed and 2 papers published.

The following year will see ongoing data analysis and paper authorship as well as a presentation 'The relationship between motor difficulties and developmental disorders' as an invited speaker at the Australasian Human Development Association Conference.

Funding: NHMRC; RPI (ongoing) 3 years \$600,000
Status: **ACTIVE – ONGOING**

96-009

Family Study of the Genetics of Osteoarthritis and Osteoporosis and related diseases

Principal Investigator:

Professor Philip Sambrook

Department Of Rheumatology,

Royal North Shore Hospital, NSW

Disorders of the musculoskeletal system that are associated with ageing, such as arthritis and osteoporosis (brittle bones), are an increasing and major problem within our population. This project investigates the causes of musculoskeletal system disorders, and in particular how people may be predisposed to developing these disorders due to the characteristics they inherit from their parents and the environmental factors associated with their lifestyle or certain medication use.

The main project incorporates three sub-studies;

- Genetics of postmenopausal bone loss study
- The effects of smoking on bone metabolism: cross sectional, within-pair comparison of smoking-discordant twin study
- The effect of anti-epileptic medication (AED) on bone mineral density (BMD), balance and fracture risk study

The study is providing insight into a number of important conditions related to musculoskeletal disease.

Three new publications have been accepted and the team plans to continue data collection for investigation of the effects of antiepileptic therapy on bone health in twins and siblings.

Funding:

NHMRC (part funding) 3 years \$75,825

Status: ACTIVE – ONGOING PROGRAM

longitudinal bone growth by studying male-female co-twin pairs.

Males have larger and wider bones that contribute to a lower risk of fractures compared to females. This sex difference in bone structure is considered to be negligible before puberty and emerges at puberty due to the increase in testosterone in males resulting in bone being laid down on the outer (periosteal) surface, thus widening the bone. The researchers compared the lengths and widths of bones at the lumbar spine and peripheral sites in boy-girl twin pairs and report that differences in bone widths, but not lengths at the arms, legs and lumbar spine, are present before puberty. Therefore the greater bone strength in males, because of their greater bone widths, is present before puberty, challenging the notion that sex differences in bone strength are only driven by sex hormones.

Achievements during this year include publication of data in peer reviewed journals and acceptance of abstracts for oral presentations at the American Society of Bone Mineral Research and the Australian and New Zealand Bone Mineral Society, both to be presented in September 2007.

Participants in this study will be invited to attend the Bone Mineral Density Department at Austin Health for a bone structure assessment using micro-high resolution peripheral quantitative computed tomography (pQCT). This is the only machine of its kind at this resolution (80 microns) in Australia, and provides detail of bone structure (cortical density and thickness, total, cortical and trabecular cross sectional area, and trabecular number, thickness and separation using minimal radiation.

Recruitment will be recommenced for this study in the following year, as well as continued analysis of serum samples for sex hormones and bone markers.

Funding:

NHMRC (Sought) 2008-2010 \$450,000

Status: ACTIVE – ONGOING PROGRAM

96-001

Bone Mass in Adolescent Male-Male and Male-Female Twin Pairs

Principal Investigator:

Professor Ego Seeman

Endocrine Centre of Excellence , VIC

The overall aim of this study is to determine the timing and magnitude of the sexual dimorphism in radial and

2002-005

Common Baldness, Dandruff and Greying of Hair in Twins

Principal Investigator:

Rodney Sinclair

St Vincent's Hospital, VIC

Hair loss that follows a characteristic pattern on the scalp, known as Androgenetic Alopecia or pattern



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baldness, occurs in both men and women. It is more prevalent among men and is the most common form of balding in Australia. The causes of the condition are complex and are not completely understood. While hereditary factors are known to be involved in the onset of male pattern baldness, the complex nature of their role is the subject of ongoing research. Less is known about the factors that cause pattern hair loss in women, since little research has been done in this area until recently. More work is needed to determine whether the same causes and genetic factors underlie both male and female androgenetic alopecia. The researchers hope to learn more about the way genes influence pattern balding in both sexes by studying hair thickness and hair loss in male and female twins.

This study is also investigating how differences in hair thickness are related to the development of dandruff (seborrhoeic dermatitis) and grey hair, as well as exploring the possibility of links between hair loss and some cancers. A recent study among Australian men found that men with prostate cancer are more likely to be bald on the crown of their head. This study will help us learn more about that association and provide information about the relationship between hair loss in women and cancer risk, particularly for breast cancer. As pattern balding means the scalp receives greater exposure to the sun, the researchers will also be looking at its effect on risk for the development of skin cancer and sunspots (solar keratosis) in both sexes.

The researchers have now completed an evaluation of women aged 50 and over with respect to hair loss and plan to review the situation in men.

Funding: Pending

Status: ACTIVE – RECRUITING

81-001

Teeth and Faces of Young Australian Twins

Principal Researcher:

Professor Grant Townsend

The University of Adelaide, SA

The overall aim of this project is to determine how genetic and environmental factors contribute to variation in different dental phenotypes using data obtained from

twins and other family members. The longer term aim is to identify the key genes that are associated with human dental development.

This study has implications in the fields of general biology, physical anthropology, and clinical dentistry (including forensic odontology). The researchers have a particular interest in the determination of body symmetry and studying the teeth of twins provides an opportunity to unravel basic biological mechanisms associated with the determination of laterality in humans. As more knowledge is gained about the role of genetic factors in determining variation within the human dentition, the researchers will be in a much better position to apply these findings to the prevention and management of developmental disturbances, including dental malocclusion.

The researchers have been able to reach the original target of recruiting around 250 pairs of twins, as well as other siblings, into the longitudinal study of dental development. Most of the twins have been examined on 3 separate occasions, at the primary, mixed and permanent dentition stages. The researchers have collected buccal cells for DNA extraction and plan to carry out genome scanning studies subject to funding. The researchers have continued to publish findings from studies in international journals and present work at international meetings. An exciting recent development has been the establishment of an international collaborative centre in dental morphology and clinical phenotyping, involving Profs Townsend (Australia), Brook (UK) and Alvesalo (Liverpool). Prof Townsend is currently in Liverpool on study leave, working with Brook and Alvesalo.

Collaborative projects are being planned in Liverpool whereby state-of-the art 2D and 3D systems of data acquisition, based on digital imaging and laser scanning, will be applied to dental models of the Australian twins, to enable more detailed descriptions of dental morphology and more incisive genetic analyses.

Funding:

NHMRC

2001-2005

\$645,000

Status: ACTIVE – ONGOING PROGRAM

2006-005

Compromised or competent? A longitudinal study of twin children's social competencies, friendships and behavioural adjustment.

Principal Investigator:

Professor Karen Thorpe

Queensland University of Technology, QLD

Twinning presents a unique situation in early childhood because twin children share a social and learning environment and are rarely apart. This study asks whether these circumstances compromise (Risk Hypothesis) or promote (Competency Hypothesis) the developmental progress and behavioural adjustment of twin children. This study examines the social relationships of twins across the preschool year through the key transition point of school entry

The central aims of the study are:

- To measure the social and behavioural competencies of twin children in early childhood and compare these with singleton age peers
- To examine the factors associated with peer relationship and friendship formation for twins, and a comparison group of singletons, in the preschool year and at school entry
- To identify the mechanisms that link twinning, social competency, social interaction and behavioural adjustment across the preschool year through to school entry
- To identify factors associated with risk and resilience in twin children's social and behavioural adjustment and adaptation
- To examine process and context in twin children's social interactions

This study makes key contributions to:

- Theoretical knowledge regarding the formation of children's friendship. Twins are a natural control for family background, level of physical and behavioural similarity (identical/ non- identical) and sex (same sex/opposite sex pairs). Comparison within twin pairs provide the opportunity to understand the influence of family relationship, similarity and sex combination of pairs on social competency, number and type of friendships

- Theoretical and applied knowledge about twin children's development and well-being. The study utilises a nested, longitudinal design which allows an innovative combination of methodologies. In this way it examines two hypotheses: (1) Psychopathology/ Risk: in a group of children who commence life with significantly increased levels of biological and social adversity (2) Competency/Resilience: in a group of children whose close relationship with another might afford unique opportunities for social learning. Findings will guide parents, teachers and health professionals in practice, intervention and policy.
- Theoretical and applied knowledge about development, learning and transition in the Early Years. Research indicates the importance of this period for life-long emotional, developmental and learning trajectories. Transition to school is a critical focus point in which the importance of family relationships and early learning experiences become apparent. The research provides data on twin children's transitions to school and more broadly informs understanding of the importance of social relationships in this transition.

Questionnaire data have been collected on 200 twin pairs and 64 singleton controls. To date, observational data have been collected on 58 twin children in pre-schools and the first year of school. Data collection will be completed in 2008 and analyses and writing for publication will continue throughout 2007-2009.

Funding:

Australian Research Council 2006-2008 \$290,000

Status: ACTIVE – RECRUITING

2004-001

Tooth Emergence and Oral Health in Twins and Their Families

Principal Researcher:

Professor Grant Townsend

The University of Adelaide, SA

At present, little is known about how important genetic factors might be in human tooth eruption. This study is the first large scale study in humans that specifically addresses this issue, which is of fundamental biological and clinical importance. The researchers are also studying the possible association between tooth emergence and oral colonisation with decay-producing



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Toothy grins: helping researchers understand tooth emergence

bacteria, and also how these bacteria are transmitted between family members. The outcomes of these studies should have direct implications for oral health strategies. Knowledge of the timing of initial colonisation with mutans streptococci (MS) will provide important guidelines about the most effective period for intervention to reduce cariogenic bacteria and prevent early childhood caries. By studying transmission of MS between all family members, the researchers will clarify the importance of paternal/sibling transfer, in addition to the recognised role of maternal transfer. This may lead to a broadening of the preventive strategy for reducing caries risk in children.

There are two main aims of this study. The first is to use multivariate modelling approaches to determine the relative contributions of genetic and environmental factors to variation in emergence of primary teeth in a large sample of twins. The second aim is to find out what the relationship is between the timing of emergence of the primary teeth and the colonisation of the oral cavity with mutans streptococci (MS), key organisms in the initiation of dental caries.

The most significant achievement during this period was reaching the target of recruiting over 500 families into the study. The researchers have already commenced preliminary analyses of some data, published some findings in international journals, and made presentations at local and international meetings.

Subject to continued funding, the researchers plan to undertake more detailed analyses of data during this period to address key objectives.

Funding:
NHMRC 2005-2007 \$514,000
Status: ACTIVE – ONGOING PROGRAM

96-007

Genetic epidemiology of endometriosis

96-007-2

Genes behind endometriosis

Principal Researcher:

Dr Sue Treloar (Visiting Scientist) and

Dr Grant Montgomery

Queensland Institute of Medical Research, QLD

Endometriosis is a common and complex condition affecting around 10% of women in the reproductive years, and causes significant disturbance because of pain symptoms, sub-fertility, treatments and hospitalisation resulting in time off work. The first twin study on this topic showed that endometriosis is influenced by genes as well as environment. Candidate gene studies have not yielded reliable results to date. The researchers have published significant linkage to a region on chromosome 10, to which twin and sibling pairs have contributed, and are fine mapping this region in order to find the genetic variants responsible. The aim of these studies is to identify genetic variants predisposing women to endometriosis. The researchers have recruited the largest collection of families with sisters diagnosed with endometriosis in the world and are collaborating with other major research groups internationally to achieve the study's aim.

The researchers hope to obtain funding to conduct a genome-wide association study for endometriosis, as samples are ready and this strategy is proving successful for other complex disorders.

96-007-3

Antenatal, childhood and adolescent risk factors for endometriosis

Principal Researcher:

Dr Sue Treloar (Visiting Scientist) and

Professor Adele Green

Queensland Institute of Medical Research, QLD

The aim of this study was to identify risk factors for endometriosis. The study was conducted by Tanya Bell (PhD candidate) as a case-control questionnaire. The study involved cases from QIMR's large study of endometriosis. Participants were selected because they had no family history of endometriosis and

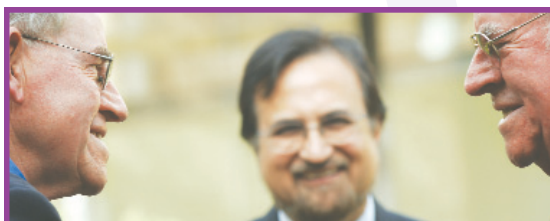
twins were also involved as controls. Mothers of cases and of twins were also asked to complete a questionnaire about their antenatal experiences and early childhood of the twin. The study is now completed and Tanya Bell was awarded her PhD; additional papers are planned.

Funding:
 NHMRC 2005-2007 \$247,375 pa for 3 years
 NIH 2007-2011 \$3 million (USD)
Status: ACTIVE – WRITING UP

2005-003

The Older Australian Twins Study (OATS)

Principal Investigators:
Prof Perminder Sachdev & Dr Julian Trollor
 Neuropsychiatric Institute, Prince of Wales Hospital, NSW



ATR members David and Denis Lynch consider their effort as Professor Perminder Sachdev looks on (Photo courtesy of Britta Campion)

OATS is a multi-centre study (NSW, Qld & Vic). Over a period of four years, participants are asked to undergo medical and clinical neuropsychological assessments, to provide a blood sample, have an MRI brain scan and answer questions about their health, lifestyle, memory and thinking. The researchers hope the study could eventually become longitudinal, following the same group for many years. Ideally, the results may be used to develop strategies for the prevention of dementia.

The research aims to measure environmental influences such as lifetime physical and mental activity, physical and psychological trauma, socioeconomic environment, alcohol and drug use, occupational exposure, and nutrition. It will also aim to determine how biological factors such as hypertension and antioxidant levels interact with genes to influence brain ageing.

To date in NSW, 133 participants have been recruited and 90 have been assessed. The interstate centres in Brisbane and Melbourne are currently being set up and expected to be in operation within the next month.

Goals for the following year include commencement of participant recruitment in Qld and Vic; commencement of year 2 participant assessment in NSW; preliminary statistical analyses; manuscript preparations of relevant findings and; conference presentations of relevant findings.

Funding:
 NHMRC/ARC 2007 – 2011 \$2,000,000
 (Ageing Well/Ageing Productively Grant)
Status: ACTIVE – RECRUITING

2001-002

How do interactions between genes and specific environmental risk factors cause eating disorders in women?

Principal Investigator:
Associate Professor Tracey Wade
 Flinders University, SA

This study is an examination of how specific environmental influences interact with genetic vulnerability to cause eating disorders in women.

The study has found that up to 8.7% had a significant eating disorder in their lifetime. The importance of understanding the causes of eating disorders is imperative given that they carry a high health cost.

Over the last 2 years a number of publications from the project have been accepted in international journals. The researchers plan to continue to produce publications from the data.

Funding:
 NHMRC 2005-2007 \$263,500
Status: ACTIVE – DATA ANALYSIS

2004-007

Risk factors for the development of eating disorder phenotypes and endophenotypes in adolescent twins

Principal Investigator:
Associate Professor Tracey Wade
 Flinders University, SA

The overall aim of this study is to investigate the mechanisms by which different environments, temperaments and genes work together to cause



SCIENTIFIC MERIT

Collaboration with researchers applying to the ATR to ensure that projects are of significant scientific merit and are appropriately described to ensure potential participants are able to provide informed consent

eating disorders. The reason the researchers follow the twins over 2 years, with a specific focus on the 12.5 to 15 years age range, is because this is the greatest period for risk of emergence and growth in eating disordered behaviour.

Anorexia nervosa and bulimia nervosa are eating disorders that affect mainly young women. In both disorders, young women judge their self-worth in terms of their weight and shape, and thus acquiring an "acceptable" weight or shape becomes of supreme importance. Eating disorders are extremely difficult and costly conditions to treat, and are associated with high mortality, and a high level of disability. Around 10% of adolescent girls will be affected by eating disorders. Given the seriousness of the consequences of eating disorders, a better understanding of the causes of eating disorders that can recommend specific prevention approaches is urgently required.

The 3-year grant commenced in March 2005, when a full time research assistant was appointed to the project. 699 twins have been interviewed (350 twin pairs, 172 MZ, 149 DZ, 29 unknown zygosity), and a second wave of follow-up interviewing has now begun.

Major goals for the next year are to complete second wave of interviewing, to write up two publications from second wave, to send out newsletter to all participants and to obtain further NHMRC funding for 2008.

Funding:
NHMRC 2005-2006 \$225,000
Status: **ACTIVE – RECRUITING**

90-001

Dietary Interventions and bone mass: Prospective Studies in Female twins (Factors in gain and loss of bone in young, menopausal, and elderly twins)

90-001-2

The effect of long-term calcium supplementation on bone densitometry in young female twins

Principal Investigator:
Professor John Wark
The University of Melbourne, VIC

Both these studies aim to use twins to test whether taking a daily calcium tablet will improve peak bone mass and strength of their bones. This is conducted by randomly selecting one twin to receive the calcium tablet and the other to receive the placebo, both of which are entirely safe to consume. The study required follow-up over a period of 3-4 years. Along with collecting health data through questionnaires, blood pressure and bone density scans were conducted every 6 months.

Status: **ON HOLD**

96-005

Risk genes for osteoporosis and other common diseases: a twin approach to interval mapping of loci

Principal Investigator:
Professor John Wark
The University of Melbourne, VIC

In essence, the aim of this study is to identify genetic markers associated with bone mineral density (and, hence, with osteoporotic fracture risk) and other quantitative traits related to common diseases (cardiovascular, respiratory, gastrointestinal, muscular skeletal and nervous systems and of the skin and metabolism).

The ongoing research program involving female twins has provided phenotypic data on more than 800 twins and more than 300 family members. Among these, dizygotic pairs will be most informative in interval mapping of loci for quantitative traits such as bone density, body fat cardiovascular, respiratory, gastrointestinal, muscular, skeletal and nervous systems and of the skin and metabolism.

To date, the researchers have studied approximately 500 dizygotic female twin pairs aged 10 to 92 years. Over 50% have been studied longitudinally.

This project is currently on hold due to lack of funding

Status: **ON HOLD**

98-007

A study of the heritability of balance in a cohort of twins

Principal Investigator:

Professor John Wark

The University of Melbourne, VIC

Familial influences on lower limb balance may contribute to the familial clustering of hip fractures. The results of this study will have important potential implications for the genetic epidemiology of falls and fractures.

The aim of the project is to investigate genetic and environmental influences on balance measures in monozygotic (MZ) and dizygotic (DZ) female twin pairs.

At the commencement of these studies, there was a need to establish retest reliability of balance and related measures used in subsequent studies. A sample of healthy women representative of the wide age range of participants was evaluated. Retest reliability of healthy women tested one week apart revealed acceptable levels of reliability on clinical and laboratory measures lower limb strength, physical activity, gait, and balance under static and dynamic conditions.

A number of presentations at international conferences were held over the last 2 years and a final PhD thesis is currently under examination.

Funding:

Osteoporosis 2004-2005

Australia

Scholarship
and

National Ageing 2006

Research Institute

(Public Health Division)

Total \$22,000

Status: ACTIVE – WRITING UP



Dr Sandra Petty and Professor John Wark measuring the bone density of ATR member David Keys

2004-003

The Effect of Anti-Epileptic Medications on Bone Mineral Density, Balance and Fracture Risk – A Twin and Sibling Study

Principal Investigator:

Professor John Wark

The University of Melbourne, VIC

Previous experience has shown that there may be a risk of osteoporosis associated with the use of anti-epileptic drugs (AED). Bone disease and fracture risk are an important issue for patients taking anti-epileptic medications. Previous research has not been conclusive about this link. In this study, the researchers aim to avoid previously encountered problems with the control group by involving twin sisters, or brothers, or matched sister or brother pairs within 3 years of age, one of whom is using anti-epileptic medication. A "control" group is used in a study to compare results of patients on a particular medication with the results of a control person, who has not taken the medication.

The purpose of this project is to examine whether anti-epileptic medications (AED) have an effect on bone mineral density, balance and fracture risk.

The twin and sibling model, controls well for many genetic and environmental factors and allows for a more powerful study to investigate these important effects.



2007 SCIENTIFIC MERIT

Collaboration with researchers applying to the ATR to ensure that projects are of significant scientific merit and are appropriately described to ensure potential participants are able to provide informed consent

The study is part of a PhD program undertaken by Dr Sandra Petty.

Dr. Sandra Petty was awarded the following:

- 2007 **James Lance Young Investigator Award**
Best Poster by PhD student, Australian and New Zealand Association of Neurologists, Annual Scientific Meeting
- 2006 **James Lance Young Investigator Award**
Best Poster by PhD student, Australian Association of Neurologists, Annual Scientific Meeting

Two publications have recently been accepted.

Funding:
NHMRC Project grant 2006-2008 \$459,750
400089
Status: **ACTIVE – RECRUITING**

To date, data has been analysed for 20 pairs of twins. This has provided assistance in deciding which assays to run in all smoking bone studies. The analysed data from 20 discordant pairs were used for a poster presentation at the 2006 ANZBMS/IOF combined meeting.

Calcium absorption testing on 18 twins currently involved in this study as well as analysis of blood and urine samples for bone formation and resorption markers and hormones levels will commence this year.

2004-004 (2)

Smoking cessation and indices of bone health: a co-twin trial

Principal Investigator:
Professor John Wark
The University of Melbourne, VIC

This project will address two key questions: – What is the mechanism of the association between smoking and osteoporosis? and; Are the abnormalities in bone and mineral metabolism associated with smoking reversible following smoking cessation?

Understanding the mechanism(s) will help to provide a rational basis for efforts to counter the adverse effects of smoking on bone (even if those effects are shown to be reversible with smoking cessation, many smokers find themselves unable to quit). Moreover, prospective evaluation of the reversibility of the smoking-associated bone disorder will provide an essential evidence-base to guide public health approaches and individual patient management aimed at preventing smoking-related osteoporotic fractures. These aims are based on the hypotheses that cessation of smoking is associated with changes in bone turnover markers and hormones (which are predictive of improved bone health). These changes in biochemical and hormonal indices associated with smoking cessation are not explained by nicotine withdrawal.

Funding:
These studies represent 2 of the 3 sub-studies which received NHMRC funding in 2003 to the value of \$635,000 under the Research Program entitled "Does quitting smoking reduce the risk of osteoporosis"
Status: **ACTIVE – RECRUITING**

2004-004 (1)

Cross-sectional, within-pair comparison of smoking discordant twins

Principal Investigator:
Professor John Wark
The University of Melbourne, VIC

The aim of this project is to cross-sectionally characterize the association between smoking indicators of bone health in women and men using a co-twin model in smoking-discordant same-sex twins aged 40 years and older. The researchers will measure and compare within discordant pairs: bone mineral density (BMD) at major skeletal sites, biochemical markers of bone turnover, relevant hormones, diet and lifestyle including detailed smoking history, soft tissue composition by DXA, height, weight and body mass index (BMI), vitamin D status, intestinal calcium absorption, reproductive history, including details of menstrual history and menopause.

These aims are based on the following hypotheses – that there are significant within-pair differences in BMD related to smoking behaviour, and that BMD difference within pairs of smoking-discordant twins are explained by differences in determinants of BMD.

88-001-4

Genetic and environmental determinants of tobacco and alcohol use trajectories into adulthood: a prospective twin study

Principal Investigator:

Dr Vicki White

**Centre for Behavioural Research in Cancer
The Cancer Council of Victoria, VIC**

Smoking is an important cause of preventable mortality and morbidity in later life, hence the need to understand the factors associated with its uptake and establishment. As most previous twin studies have not investigated the role of genes on smoking uptake while controlling for the influence of psychosocial factors on initiation, our current understanding of how genes and the environment interact in the development of smoking behaviours is limited. This study is one of the few longitudinal twin studies of smoking uptake and is uniquely placed to investigate this issue.

The researchers have conducted analyses examining the role of genes and friends smoking on smoking behaviour. Being concordant for having peers who smoked was a predictor of concordance for smoking and after adjusting for peer smoking, identical twin pairs were no more alike than non-identical twin pairs for smoking in adulthood. An article reporting these findings has been submitted for publication.

In addition the researchers identified and interviewed a group of identical twin pairs who were discordant for smoking during adolescence and young adulthood. The interviews showed that twins thought their different smoking status was connected to their different friendship groups and the development of different identities. Smoking respondents gravitated to the behaviours and images of the peer group who smoked while many non-smokers felt strong pressure from their peers to not smoke. An article reporting these findings has been accepted for publication.

Funding:

NHMRC
400089

2003-2005

\$138,250

Status: ACTIVE - DATA ANALYSIS

96-0104

The genetic determinants of working memory, information processing and intelligence in twins

Principal Investigator:

Dr Margie Wright

Queensland Institute of Medical Research, QLD

This study aims to identify genes influencing cognitive ability by using varied measures of cognition in genetic linkage and association analyses, in a large sample of twins. The preliminary linkage scans have shown significant linkage to a region on chromosome 2. The researchers intend to fine-map this region to refine the area in which the functional gene is located, and will also use multivariate linkage analysis to increase the statistical power of finding a gene, and help define the phenotype related to the gene.

This study is the first in the world to find significant linkage for IQ. The dataset is one of only 2 such in the world (based on sample size, range & type of measures). Identifying genes for cognitive ability using healthy subjects is important in understanding individual differences in normal cognitive functioning, but it may also provide clues into the underlying mechanisms of impaired cognitive ability. Diverging conditions such as reading disorder, schizophrenia, depression, alcoholism, and dementia all share deficits in cognitive ability.

Linkage analyses of the main cognitive phenotypes were completed, genotyping and association analysis for several genes was completed, and the researchers have begun data cleaning of the SNP data from the 100K SNP chip.

The objectives for the following year are to:

- continue testing twins/sibs
- extend the genetic linkage analyses to the information processing and ERP measures and submit these findings for publication
- undertake association analysis using available genotyping and submit findings for publication
- begin work on the genome wide association scan.

Funding:

Australian Research
Council

2006-2008

\$500,000

Status: ACTIVE – ONGOING PROGRAM



SCIENTIFIC MERIT

Collaboration with researchers applying to the ATR to ensure that projects are of significant scientific merit and are appropriately described to ensure potential participants are able to provide informed consent

PUBLICATIONS

Enabling Grant Goal: Increase the number of peer reviewed articles to 50 per year

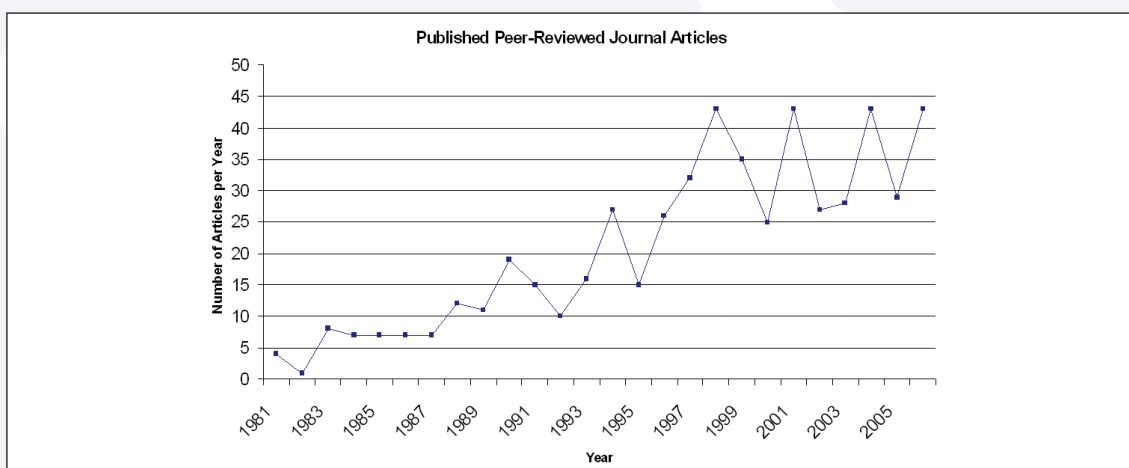
An important measure of the output of the ATR is the number of publications arising from studies supported by the facility. To date 576 peer-reviewed publications and 496 conference proceedings have arisen from ATR supported projects. Appendix 2 provides a full listing of publications since 2003.

Table 2: Publications arising from ATR supported projects since 1981

	Completed	In press	Submitted	In preparation
Book	3			
Book Section	50	3		
Published Abstracts	72			
Conference Proceedings	496			
Peer Reviewed Publications	576	8	2	10
Thesis	11			
Reports	6			
Newspaper Articles	7			
Magazine Articles	4			

The number of peer reviewed publications has increased steadily and in recent years has averaged about 35 per year.

Graph 1: Number of Articles Published per Year



ATR COMMUNITY UPDATES

Enabling Grant Goal: Open, professional network of researchers

The ATR continues development as an open, professional network of current and prospective researchers from a range of disciplines. Regular email communication is used to announce publications and other important documentation, update researchers regarding ATR administration and governance, advertise conferences and employment opportunities, facilitate collaboration and describe funding opportunities, etc. The e-mail

distribution list covers researchers, stakeholders and other interested parties.

An important mechanism for communication between the ATR and researchers who currently or potentially utilise the facility has been the introduction of ATR Community Updates.

These updates are provided roughly 3 – 4 times per year and ensure that researchers are kept up to date with the latest activities of the ATR. It is also a valuable mechanism to disseminate and share resources and communicate new and improved procedures.

RESEARCHER TRAINING

Enabling Grant Goal: Facilitate training and development of Australian twin researchers

Enabling Grant Goal: Hold Annual Twin Workshops

The ATR undertakes annual activities to facilitate the training and development of Australian researchers in the methodology and practice of studies involving twins. These activities include presentations at international and national conferences, and the coordination of workshops and seminars aimed at new and existing researchers. This process is considered fundamental to ensure the vitality and quality of twin research using the ATR.

During the period July 2005 – June 2007 the following twin workshops were conducted:

GeneMappers 2005 incorporating the Australasian Twin Registry Conference

The ATR co-sponsored GeneMappers05, a scientific meeting of international and local experts in twin research and genetic epidemiology, held at Mount Buller on 23rd – 25th November 2005. Rolled into this important event was the ATR's 9th *It Runs In The Family* conference.

Speakers included Professor Pak Sham from the Institute of Psychiatry at King's College, London; Dr Shaun Purcell from the Psychiatric and Neurodevelopmental Genetics Unit at Massachusetts General Hospital; and Associate Professor Karl Broman from Johns Hopkins Bloomberg School of Public Health, Baltimore. The ATR contributed to the organisation of the three-day event and supported the attendance of international speakers.

Genetics for Epidemiologists and Epidemiology for Geneticists workshop 2006

The ATR, together with the Australian Medical Bioinformatics Resource (AMBeR) organised a one-day workshop on September 17th immediately prior to the Australasian Epidemiological Association (AEA) conference in Melbourne. The workshop presented the opportunities that new genetic knowledge, techniques and approaches have opened up for epidemiological research, and the potential for researchers to use nationally funded resources and facilities.

Professor Tom Mack from the University of Southern California presented exciting perspectives in his keynote talk on the many possible designs for twin research, using example of early life risk factors for diseases such as multiple sclerosis and breast cancer. Australian speakers included Sam Berkovic (recently awarded the 2005 Curtin Medal for Outstanding Contribution to Australian Medical Science, Austin Health/University of Melbourne), Lyle Palmer (WA Institute for Medical Research/University of Western Australia), Melanie Bahlo (Walter and Eliza Hall Institute), Sue Forrest (Australian Genome Research Facility), Stuart Macgregor and David Duffy (Queensland Institute of Medical Research), and Graham Giles (Cancer Council Victoria).

Twins and Child Health Research Workshop 2007

Drs Ruth Morley and Supriya Raj from the ATR (**match**) convened a workshop in Melbourne on April 16th. The workshop had three main objectives:

- to increase awareness of research opportunities from studying twin children
- to inform researchers of child twin cohorts in Australia that can be accessed by researchers
- to discuss whether twin cohort facilitators should ask parents of twins to collect prospective information and if so, what information should be collected.

Invited speakers presented on topics ranging from twin studies and design issues to data analysis and generalisations from twin studies. Also discussed was the development of speech, language and behaviour in twins. This workshop was well attended by prominent researchers working in various areas of child health research. Discussion at the end of the workshop was on whether twin child cohorts should collect prospective data. This stimulated much discussion and will be further explored with a smaller working group.

A manuscript is in preparation, detailing the various types of twin studies discussed and the strengths and weaknesses of twin research.

Statistics Short Course 2008

In response to feedback received at the previous "Genetics for Epidemiologists" workshop, planning for a 'hands-on' statistics training session is underway. This 5 day intensive course will feature Mendel and other state-of-the-art statistical genetics methods for detection



SCIENTIFIC MERIT

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of genetic loci for complex traits. To be held in September, 2008 (venue to be advised), the short course will be presented by instructors from the University of California, LA Department of Human Genetics.

The ATR set up information booths at the following expos and was able to make contact with new researchers who were considering utilising the ATR in their studies.

Australian Science Festival 2005

Canberra, 17th–21st August, 2005

Australian Medical Research Week Expo 2005 and 2006

Federation Square, Melbourne, 5th June, 2005 and 4th June, 2006

National Heart Foundation Conference 2006

Sydney, 23rd–24th March, 2006

11th International Congress of Human Genetics (ICHG) 2006

Brisbane, August 6th–10th, 2006

In addition, symposia and sessions at various international conferences

Australian Institute of Ultrasound 2005

Presentation on **match**

Brisbane, Queensland, 22nd May, 2005

Australian Epidemiological Association 2005

Newcastle, New South Wales, 6th–7th October, 2005

A special ATR workshop on twin methodologies '*The Australian Twin Registry: A Valuable Resource for Epidemiological Research*' was held at the conference. Chaired by Professor John Hopper, speakers included Dr Sue Treloar, Dr Katrina Scurrah, and Ms Katherine Morley.

10th Annual Conference of the Perinatal Society of Australia and NZ 2006

Presentation of **match** project

Perth, Western Australia, 3rd–6th April, 2006

Australian Epidemiological Association 2006

University of Melbourne, Victoria, 18th–19th September, 2006

Sponsored concurrent paper session chaired by Professor John Hopper, which included presentations from US researchers Tom Mack and Wendy Cozen.

The International Congress on Twin Studies 2007

Ghent, Belgium, 7th–10th June, 2007

The conference was attended by a range of researchers who have worked with the ATR on their studies. The ATR and Dr Katrina Scurrah convened a symposium on '*Novel Ways to use Twins in Epidemiology*' and **match** presented a poster on their work. Professor John Hopper presented a talk '*Can twin studies be used to infer causation?*'. Professor Nick de Klerk (WATCH) presented a paper '*Variance components for exhaled Nitric Oxide in twin families*' and chaired the session on '*Substance use / abuse and pharmacogenetics*'.

GeneMappers 2007

The ATR is a conference sponsor for GeneMappers 2007, which is being held at Royal on the Park in Brisbane in August, 2007

Professor John Hopper is chairing the session '*Twins and Association Studies*'

RESEARCH TRAVEL GRANT SCHEME

In addition to coordination of twin workshops and presentations to facilitate researcher training and development, the ATR actively encourages researchers to present their work at international conferences in order to spread the word regarding the value and power of twin studies.

To this end, the ATR sponsors a Research Travel Grant Scheme which encourages the growth and development of twin research in Australia by:

- facilitating the training and development of Australian researchers in the methodology and practice of studies involving twins by offering financial support to attend relevant international research workshops and conferences
- fostering an active network of researchers from a range of disciplines and
- promoting the presentation of ATR studies at scientific conferences.

The Research Travel Grant Scheme awards partial funding within the range of \$300 – \$2000 for relevant travel costs. Applications are competitive and open to all Australian-based researchers involving twins in their studies. Selection of successful candidates is made on the basis of the:

- ability of the specified event to benefit a research career using study methodologies incorporating twins;
- extent to which recipients will be publicising the benefits of studies using twins among the broader research community and
- availability of other sources of funding to the recipient.

Successful applicants are required to submit a Travel Report detailing professional and personal gains from the funded travel. This is published on the ATR website www.twins.org.au

The successful applicants for the first three rounds of the scheme are named below. Round 4 is planned for late 2007.

Research Travel Grant Scheme – Successful Applicants Round 1 (Early 2006)

Abdullah Sheikhi

Abdullah went to Boulder, Colorado on March 6-10th, 2006 to attend the 19th International Workshop on Methodology of Twin and Family Studies. Abdullah is undertaking a PhD at the Curtin University of Technology, School of Psychology, WA.

Beben Benyamin

Beben attended a short course on using FBAT and PBAT at the Harvard School of Public Health, Boston MA, on the 12-13th June, 2006. Beben is undertaking a PhD with the Queensland Institute of Medical Research, in Genetic Epidemiology.

Brendan Zietsch

Brendan is currently undertaking a PhD through the University of Queensland, School of Psychology, Department of Social Sciences. Brendan travelled to Boulder, Colorado on March 6-10th, 2006 to attend the 19th International Workshop on Methodology of Twin and Family Studies.

Jonathan Hansen

Jonathan attended the 28th Annual Meeting and Pre-Meeting Satellite Symposium of the Association for Chemoreception Sciences. He was also invited to present results of an ongoing twin study at the Monell Chemical Senses Centre in Philadelphia after the conference. Jonathan is undertaking a PhD with the Queensland Institute of Medical Research, in Genetic Epidemiology.

Mohamed Dirani

Mohamed is a PhD student with the Department of Ophthalmology at the Centre for Eye Research Australia (CERA). Mohamed travelled to the 11th International Myopia Conference in Singapore on the 16-18th August, 2006. He presented results of his research into the genetic components of myopia.



SCIENTIFIC MERIT

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Sri Shekar

Sri is currently undertaking a PhD with the Queensland Institute of Medical Research, in Genetic Epidemiology. He travelled to the 67th Annual Meeting of the Society for Investigative Dermatology in Philadelphia, PEN on May 3-6th. He presented results of positive linkage of hair colour.

Research Travel Grant Scheme – Successful Applicants Round 2 (Late 2006)

Katrina Scurrah

Katrina undertook travel to the Australian Statistical Conference/New Zealand Statistical Association Conference 2006 in Auckland, New Zealand on 3-6th July, 2006. Katrina is a Research Fellow with the Department of Physiology at the University of Melbourne.

Megan McDougall

Megan was a successful recipient of a travel grant to attend the 4th International Conference on Child and Adolescent Mental Health in Mumbai, India on the 5-7th October, 2006. Unfortunately, this conference was cancelled.

Naomi Wray

Naomi travelled to the International Psychiatric Genetics Meeting in Calgliari in Sardinia on October 28 – November 1st, 2006. Naomi recently moved from the UK to join the Genetic Epidemiology Group at the Queensland Institute of Medical Research as a statistical geneticist.

Research Travel Grant Scheme – Successful Applicants Round 3 (Early 2007)

Brendan Zietsch

Brendan is currently undertaking a PhD through the University of Queensland, School of Psychology, Department of Social Sciences. He was awarded a Round 1 grant to attend the 19th International Workshop on Methodology of Twin and Family Studies (introductory level). He was awarded a second grant to attend the advanced level course on 5-9th March, 2007 in Boulder Colorado, USA.

Enda Byrne

Enda is a PhD scholar enrolled through the School of Medicine, University of Queensland. He attended the Twentieth International Workshop on Methodology of Twin and Family Studies on 5th-9th March, 2007 in in Boulder Colorado, USA.

Michelle Bockmann

Michelle is with the School of Dentistry, The University of Adelaide. She was awarded a grant to travel to the Genetic & Developmental Psychiatry Centre 8th Summer School in London on 16th-20th July 2007.

Lauren Day

Lauren is with the Department of Medicine at the Royal Melbourne Hospital. She was awarded a grant to present a poster at the 29th Annual Meeting of the American Society for Bone and Mineral Research in Honolulu, Hawaii on 16 - 19th September 2007 but was unable to attend and subsequently withdrew her application.

Ingo Helbig

Ingo is with the Epilepsy Research Centre, University of Melbourne. He travelled to the 27th International Epilepsy Congress in Singapore on 8th - 12th July, 2007. He presented his work on twin studies at the conference.

Megan McDougall

Megan is with the School of Psychology, Curtin University of Technology, WA. She travelled to the 12th International Congress on Twin Studies in Ghent, Belgium on the 7-10th June, 2007 where she presented a poster on her work. She also attended the International Society for Research in Child and Adolescent Psychopathology (ISRCAP): Thirteenth Scientific Meeting in London on the 20 - 23rd June, 2007 where she again presented a poster and also an oral presentation.

Nick Wong

Nick is with the Epigenetics Research group, Murdoch Children's Research Institute. He travelled to the 12th International Congress on Twin Studies in Ghent, Belgium on the 7 - 10th June, 2007 and presented his work.

Michelle Luciano

Michelle is with the Genetic Epidemiology Laboratory at the Queensland Institute of Medical Research. She travelled to the 37th Annual Meeting of the Behaviour Genetics Association in the Netherlands on the 3-6th June, 2007 and the 12th International Congress on Twin Studies in Ghent, Belgium on the 7 - 10th June, 2007. She presented her work in oral format at both events.

Belinda Cornes

Belinda is with the Genetic Epidemiology Laboratory at the Queensland Institute of Medical Research. She was awarded a grant to travel to the 12th International Congress on Twin Studies in Ghent, Belgium on the 7 - 10th June, 2007, but was unable to attend and subsequently withdrew her application.

PARTICIPATION

Judicious management and administration of approach to eligible twin members to inform them of a new research project, determine their interest in participation, and seek their permission to release their contact details to the researcher

PARTICIPATION IN STUDIES

The ATR acts as a recruitment and communication resource to facilitate research across Australia.

Research activities are administered by the researcher and not by the ATR. However, in some situations the ATR may administer an eligibility questionnaire to screen for ATR members with specific characteristics and expedite the activities of the researcher, or collect data itself to facilitate future research.

The range of research activities that members ultimately participate in can include:

- telephone interviews
- written questionnaires
- donating bio-specimens (blood, cheek cell swabs etc)
- undertaking physical tests (scans, measurements etc)
- taking vitamins/supplements
- providing consent to access health records or existing bio-specimens
- providing permission for researchers to discuss their health with other family members

Trust is maintained between the ATR and its members by providing potential participants with the opportunity to understand the study fully before consenting. This trust is vital to ensure that twins are willing to consider

participation in future studies, and therefore secures the continuance of the facility for other researchers.

The ATR requires transparency and use of appropriate language to clearly explain the full burden of the study to potential twin participants at the time they receive the invitation from the ATR.

ATR members are free to withdraw from a study at any time, and to decline to answer any question or to undertake any test that makes them feel uncomfortable.

ATR members display genuine willingness to help and interest in being involved in research studies. Under no circumstances are participants pressured to continue with a study just because they have already begun participation.

Serious consideration is given during the application review process as to whether the ATR will find it necessary to approach twins who are known to have been in one or more previous studies, or are known to be in the group that is being approached for a current study.

The ATR manages the approach to twins in a manner that is sensible, appropriate, fair and impartial. The ATR takes into account at all times the level of burden of a study and takes measures to prevent over-approach. This balancing of the needs of twins and researchers can mean that researchers are delayed in accessing certain groups of twins.



PARTICIPATION

Judicious management and administration of approach to eligible twin members to inform them of a new research project, determine their interest in participation, and seek their permission to release their contact details to the researcher

APPROACH

The initial approach to ATR twin members is usually made via an 'Approach Package' mailed out by the ATR directly to the member (or parent/guardian if the twins are under 18).

The development of the documentation included in the approach package, and decision regarding the approach method to be utilised takes place during the application phase.

The use of clear and comprehensive documentation to invite twins to participate in the research is extremely important. This documentation is often the sole opportunity the ATR has to request participation. Therefore, careful construction of the documents is paramount to ensure that members are able to provide informed consent. Information sheets clearly state the burden of the study for participants in terms of number, likely length and location of all tasks, questionnaires, interviews, clinical testing sessions, further follow up sessions or activities and other study protocols. Information Sheets also contain contact details for the approving Human Research Ethics Committee so that in the event of any issue or problem, the twin member is able to have complaints heard and acted upon.

The Standard Approach Package comprises:

- a letter from the ATR (on ATR letterhead and signed by either the Director or Deputy Director) endorsing the study as one that has been appropriately reviewed and approved by the ATR
- a letter from the researcher and/or a detailed information sheet which explains the nature and purpose of the proposed research, the procedures that are associated with participation in the study (including specifics of who, what, why, where, when, for how long, and with what possible associated risks)

- an ATR Response Form for the member to indicate their response and provide updated contact details if necessary
- a Reply Paid envelope, addressed to the ATR.

The ATR database records the number of times each individual has been approached for participation in a study. Inbuilt processes within the database allow the selection of twins for approach if the pair:

- are eligible due to project requirements for age, gender, zygosity, location, etc.
- have not been approached within the last 6 months
- are both marked as "Active" status or in the case of simple questionnaire only studies, marked as "Questionnaire Only" status.

APPROACH VARIATIONS

In order to provide a more efficient and streamlined service for researchers, the ATR has introduced a range of variations to the Standard Approach protocol, including the ability to add a screening questionnaire, request for additional consent to access a medical record or bio-specimen to screen for eligibility, or directions for twins to access an internet-based survey. Each study is assessed on a case-by-case basis to determine the most appropriate approach mechanism.

Variation – Screening Questionnaire

If the researcher is interested in enrolling twin pairs with a particular trait, they can negotiate with the ATR to include a short screening questionnaire in the Approach Package. The screening questionnaire is mailed back to the ATR in a Reply Paid envelope, together with the ATR Response Form. It is important that the screening questionnaire is short and specific, and that the twin is informed of the possibility that they will progress to another phase of the study, depending on the results of their screening questionnaire.

Variation – Additional Consent to Access Medical Records or Bio-specimens

This variation is used where eligibility is based on the review of medical data (such as perinatal statistics) or test using an existing bio-specimen (such as an archived Pap smear, blood sample or Guthrie card). This variation takes into account the need for cost effective strategies to make prudent use of limited research funds and

allows the targeted selection of eligible members without the need for additional, unnecessary, re-testing for specific traits. Detailed information is included in the Approach Documentation that describes the process, any risks involved and their consequences (including the potential destruction of a bio-specimen during the proposed testing process).

Variation – Study Pack (Juniors and Half-Yes Eligible Only)

The ATR acknowledges that some research projects are subject to tight timeframes. In these situations, the researcher may negotiate the inclusion of a Study Pack in the Approach Package. This can only occur where the study is paper or internet-based. The standard Approach Package is used, and in addition, a Study Pack is enclosed containing the survey instrument, a detailed consent form and instructions. Members are invited to read through the Approach Package, and if they are interested in participating, are instructed to open the Study Pack and complete the activities. The ATR Response Form and study materials are returned in the Reply Paid envelope to the ATR.

Variation – De-identified Study

This variation can be utilised when the researcher does not require identified data. Study materials are internet or paper-based. It is used to reduce the work required by the twin and the researcher and is deemed a cost effective and reasonable method to collect project data.

Variation – Low Prevalence Traits

This variation is used where eligibility is based on one or both of the twins displaying a particular trait or medical condition, which has a very low prevalence in the general population. In these situations, approaching a large number of ATR members is required in order to ascertain a very small number of affected members. The cost of such a mailout is generally prohibitive and not considered an efficient use of valuable research dollars. To reduce costs in these situations, the standard ATR Response Form is piggy-backed onto existing bulk mail-out activities such as the annual *Twins* Newsletter. The limitation of this variation is the low frequency of bulk mailout activities, meaning that studies utilising this option must time their recruitment accordingly.



PARTICIPATION

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MAIL OUTS

A core activity of the ATR is the coordination of mailouts to prospective participants for individual studies. The number of mailouts and total number of approaches depends on the needs of the researcher. During the period 1 July 2005 – 30 June 2007, 125 mailouts were conducted, with 25,663 approaches made.

Please note this table summarises approaches for both Junior members (1 approach per family) and Senior members (1 approach per twin). The number quoted also includes reminder mailouts.

Table 1:
Mailouts 1 July 2005 – 30 June 2007

Study ID	Number of Mailouts	Total Approaches
98-001	5	68
97-001-3	1	20
94-005-2	20	5,624
2001-005-1	2	492
2002-002	2	1,321
2003-001-1	1	1,324
2004-001	26	553
2004-003	8	7,102
2004-004	6	2,612
2004-007	11	575
2005-002	1	398
2005-003	6	307
2006-001	28	3,522
2006-003	1	1,150
2006-005	3	522
2006-005-1	1	14
2007-001	4	73
Total	125	25,663

These mailouts span the 24 month period between 1 July 2005 and 30 June 2007. However, the increase in Telephone Follow Up and the new procedure for Verbal Consent introduced in 2006 has reduced the number of follow up mailouts and approaches required in the latter part of this period.

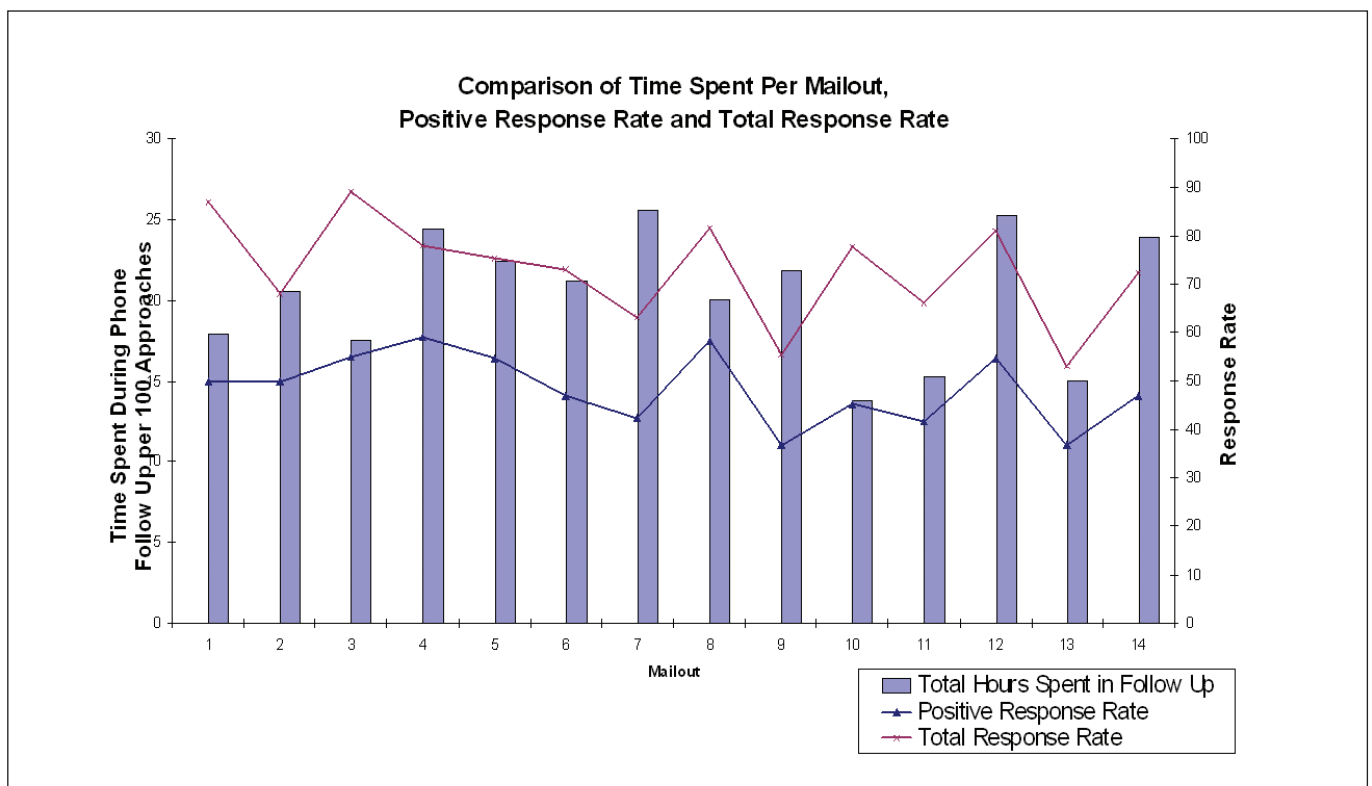
TELEPHONE FOLLOW UP

Telephone Follow Up is offered to researchers as a method of increasing overall response rates. It can be used in conjunction with Reminder Letters, however, most researchers elect to use either method as opposed to both. An analysis of response rate compared to telephone follow up hours for the *Cannabis & Mental Health* study shows that response rates track closely to the amount of time allocated to the telephone follow up effort. The table below shows that on average 16.7 hours is spent in telephone follow up per 100 approaches, equivalent to 10 minutes per approach (includes multiple telephone calls, messages and time to respond to questions). Graph 1 shows that beyond this, increasing time on follow up for each mailout does not translate to an equivalent increase in positive response (i.e. mailout 4). The graph also shows that the proportion of positive response relative to total response is fairly stable.

Table 2: Time Spent in Telephone Follow Up Per Mailout and Resulting Positive Response Rate

Mail out	Number of Approaches per Batch	Total Hours Spent in Follow Up	Total Hrs Spent in Phone Follow Up Adj for Batch Size	Avg Time Spent per Approach	# Positive Responses	# Negative Responses	# No Resp	Positive Resp Rate %	Total Resp Rate %
5	100	17.9	17.9	10.76	50	37	13	50	87
6	100	20.6	20.6	12.33	50	18	32	50	68
7	100	17.5	17.5	10.52	55	34	11	55	89
8	100	24.4	24.4	14.63	59	19	22	59	78
9	130	22.5	17.3	10.36	71	27	32	55	75
10	130	21.2	16.3	9.77	61	34	35	47	73
11	130	25.6	19.7	11.82	55	27	48	42	63
12	130	20.1	15.4	9.25	76	30	24	58	82
13	130	21.9	16.8	10.08	48	24	58	37	55
14	130	13.8	10.6	6.36	59	42	29	45	78
15	130	15.3	11.7	7.04	54	32	44	42	66
16	130	25.3	19.5	11.68	71	34	25	55	81
17	130	15.0	11.6	6.93	48	21	61	37	53
18	170	23.9	14.0	8.43	80	43	47	47	72
Average			16.7	10.00					

Graph 1: Time Spent in Telephone Follow Up Per Mailout and Resulting Positive Response Rate





PARTICIPATION

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VERBAL RESPONSE

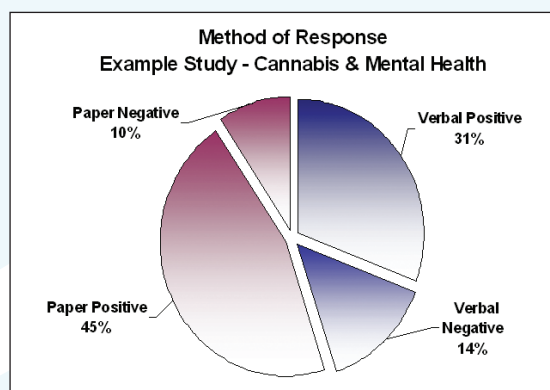
Given the commitment made to twins or parents when they register, information is kept strictly confidential and personal details are not given out without the prior consent of the individual concerned. Researchers are provided with identifying information for a particular project only if and when the informed consent of twins (or a parent/guardian in the case of twins under 18) 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 in the Approach Package documentation and endeavours to negotiate an efficient and effective approach method. However, the ATR cannot make any guarantee about the expected response rates for a study.

In 2006 the ATR instituted a Verbal Response process whereby ATR Research Assistants are able to record a twin member's response during a follow up telephone call. This can reduce the burden on the member whilst maintaining the Registry's ability to protect the privacy and confidentiality of the twin, and enabling them to make an informed response. The ATR makes it very clear that the twin is only consenting to the ATR passing contact details on to the researcher for the purposes of the study, and that more detailed information and a written participation consent form will be forwarded by the researcher. A Verbal Response is not considered sufficient for the researcher to assume informed consent for participation in the study itself.

The availability of the Verbal Response protocol for any particular study is assessed on a case by case basis, depending on the ability of the twin member to be adequately informed regarding the study verbally.

For studies utilising the Verbal Response procedure, paper based response still remains the more common method for twin members to register their response to an approach. The following Graph 2 shows an example study utilising verbal and paper response methods. Paper based response remains the more utilised method at 55% of the total response received, however, Verbal Response returns a significant proportion of the overall total positive response received. Verbal Response and Telephone Follow up have contributed to the significantly high overall positive response at 76%.

Graph 2: Breakdown of Positive and Negative Verbal and Paper Based Responses (N= 2009 responses)



RESPONSE RATES

Table 3 provides a comparison of response rates for a selection of current projects based on the selection criteria for each and the condition being studied (where M/M are male/male pairs, F/F female/female pairs and M/F male/female pairs). Twins of all zygosity types are invited to participate in each of these studies unless otherwise stated.

Response rates to Registry mailouts appear to be higher for those studies approaching either families with young twins (under 18 years old) or older, adult twins (40 years and older). Twins between the ages of 18-40 years old have the highest 'No Response' and 'Negative Response' rates and are the most difficult group to maintain current contact information for.

Negative response rates also include twins who are deemed ineligible to participate in a study based on the researchers' criteria. The high negative response rate for the *Smoking and Bone Health* study, for example, reflects the large number of older adult twins who responded to the approach indicating that neither twin smokes. Likewise, the negative response rate for the *Transition to School* study included all twins who were not eligible as they had either already started school or were not starting in 2007.

Response and participation rates vary depending on the requirements of the study, the characteristics of the group approached, and the extent of the follow-up undertaken. The instigation of phone follow-up by ATR staff to non-responders has resulted in an increase in total response

rate to Registry mail-outs. For example the studies on *Teenage Eating*, *Teenage Eating Habits*, *Molecular Genetics of Inattention*, *Brain Ageing and Cognition*, *Breast Density and Calcium*, *Vitamin D & Bone Health in Pre-teen Girls* all utilise comprehensive phone follow-up.

The figures also demonstrate that studies with a high burden of participation on the twins appear to have lower positive response rates than those with a reduced burden of participation. For example the *Calcium*,

Vitamin D & Bone Health in Pre-teen Girls study involves each twin taking twice daily tablets over a 12 month period. Of the 47 pairs approached, 40% agreed to participate and 43% declined, many stating that this was due to the burden imposed on families to participate. In contrast, the study on *Teenage Eating Habits*, which targeted a similar age group but consisted only of a telephone interview, had a positive response rate of 58%.

Table 3: Study Response Rates for a Selection of Active Studies

Study Name	Criteria	Total Pairs Approached	Positive Response Rate	Negative Response Rate	1 Twin Response Rate	'No Response' Response Rate	Total Response Rate
Juniors							
Tooth Emergence	F/F, M/M, M/F 0-1yr – Aust wide	479	66%	15%	N/A	19%	81%
Reading Ability	F/F, M/M 3.75-5yrs – Syd	315	65%	12%	N/A	22%	78%
Teenage Eating Habits	F/F 12-14yrs – Aust wide	719	58%	34%	N/A	9%	91%
Calcium, Vitamin D & Bone Health in Pre-teen girls*	Identical F/F, 9-12yrs – Syd	47	40%	43%	N/A	17%	83%
Transition to School	F/F, M/M, M/F 4-6yrs – Aust wide	495	28%	45%	N/A	27%	73%
Transition to School Phase 2	Researcher identified list	14	71%	14%	N/A	14%	86%
Molecular Genetics of Inattention	Researcher identified list	212	44%	50%	2%	4%	96%
Seniors							
Myopia and Personality	Researcher identified list	573	55%	3%	25%	17%	83%
Cannabis and Other Illicit Drug Use: A Twin Study*	F/F, M/M, M/F 25-35yrs – Aust wide	1956	27%	24%	14%	35%	65%
Breast Density: Twin & Sisters	F/F 40-70yrs – Aust wide	2477	46%	38%	5%	10%	90%
Smoking & Bone Health	F/F, M/M 40-85yrs – VIC, NSW	3036	4%	69%	2%	25%	75%
The Twin Study of Brain Ageing and Cognition*	F/F, M/M, M/F 65+yrs – NSW	146	36%	56%	2%	6%	94%

* Studies currently recruiting and undergoing follow-up to non-responders.

Strategies to increase the study response rate of twins who are being approached, and to recruit twins independent of the ATR are discussed in advance. While these strategies may or may not directly involve the ATR, the researcher must advise of any initiatives

that have been put in place (such as forthcoming publicity, interviews, articles, newspaper and radio ads) in order to facilitate collaboration and ensure that the ATR is in a position to distribute accurate information in response to queries.



PARTICIPATION

Judicious management and administration of approach to eligible twin members to inform them of a new research project, determine their interest in participation, and seek their permission to release their contact details to the researcher

APPROACH AND RESPONSE

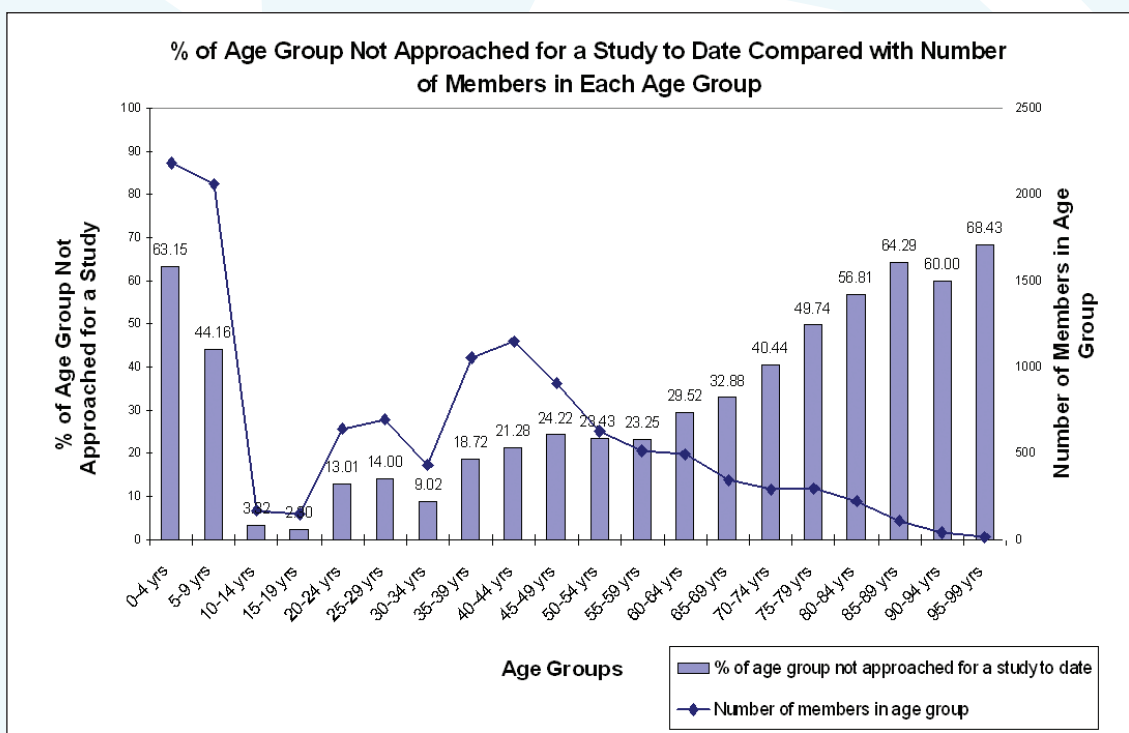
In 2006, the ATR investigated the relationship between response and approach rates to determine potential mechanisms to increase positive response.

The analysis showed that the 8120 youngest (aged under 10 years) and 1241 oldest twin pairs (aged 75 years and older) have been approached less frequently for studies than other age groups; in the latter group over 50% had not been approached at all in the past 10 years. In the other age groups, the great majority had received at least one approach regarding a study, although there were still twins who had never been approached.

Table 4: Study Response Rates for a Selection of Active Studies

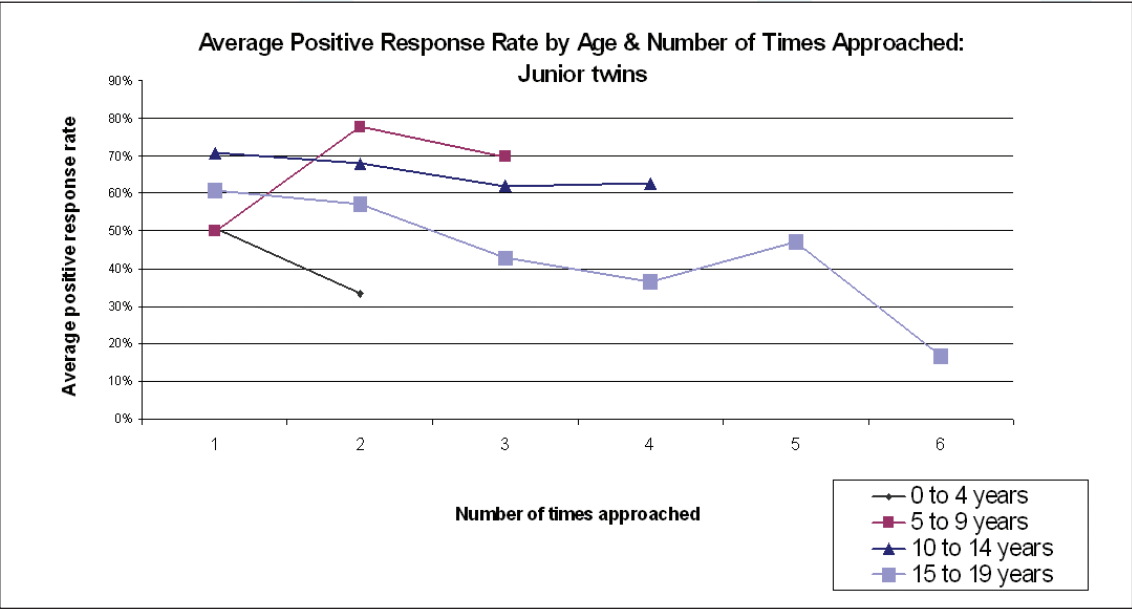
Age Group		0	1	2	3	4	5	6	7	8	9	10
(years)	N pairs	% of age group										
0 to 9	8120	42.2	41	6.6	0.2							
10 to 19	11776	2.7	53.3	26.3	10.9	6.3	0.4	0.1				
20 to 29	9448	14.2	30	24.5	14.4	8.5	4.2	2.6	1.1	0.4	0.2	
30 to 39	10439	14.2	31	25.5	13.3	9.4	3.7	2.1	0.8	0.1		
40 to 49	9136	22.5	30.5	17.3	11.9	7.7	5.5	3.2	1.1	0.2	0.1	0
50 to 59	4880	23.4	23.4	18.4	11	9.3	6.2	3.8	3.1	1.2	0.3	0
60 to 69	2713	30.8	21.4	12.9	10.2	9	6.9	5.2	2.3	1.1	0.2	
70 to 79	1313	44.6	17.3	9.7	9.6	9.4	6	1.9	1.1	0.3		
80 to 89	564	59	14.9	11.4	8.7	3.9	1.8	0.4				
90 to 99	84	61.9	31	4.7	2.4							

Graph 3: Proportion of Age Group Never Approached for a Study in Comparison to the Number of Members in Each Age Group

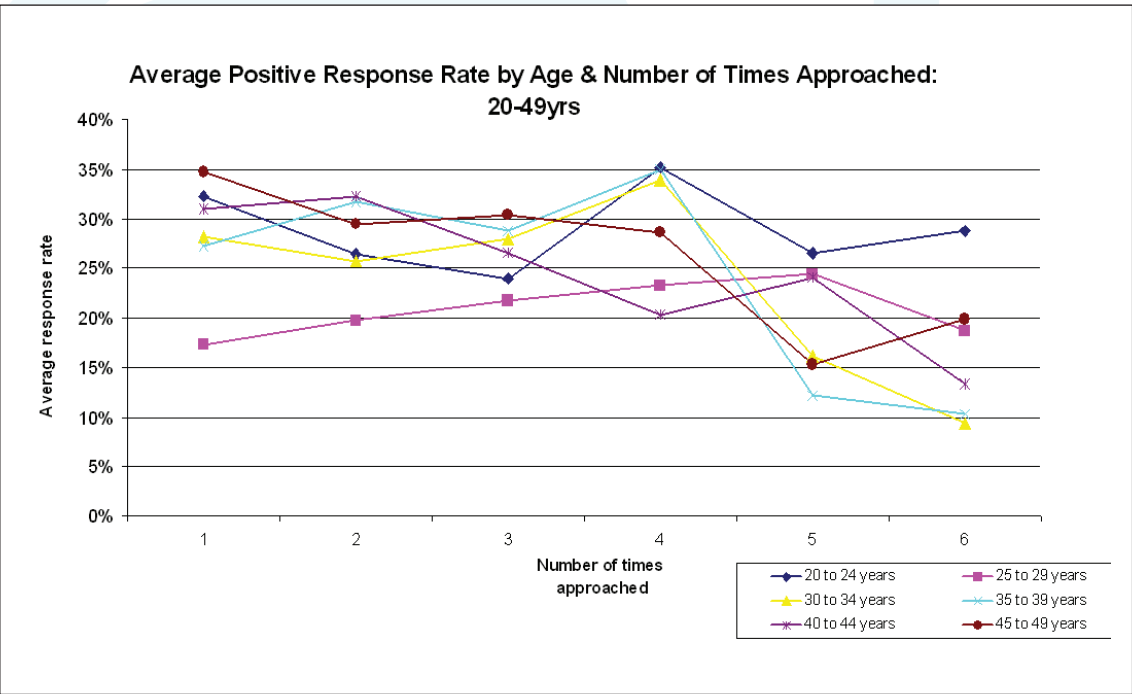


We analysed positive and negative response according to the number of approaches made, and by age group. Apart from the very elderly, the lowest positive response rate is observed in the 25-29 year old age group and the highest by 5-19 year-olds and 55-79 year olds. For all age groups, positive response declines with number of approaches, especially after a threshold of 4 approaches is reached.

Graph 4:
Positive Response Rates by Age and Number of Times Approached: Junior Members



Graph 5:
Positive Response Rates by Age and Number of Times Approached: Senior Members 20 – 49 years old

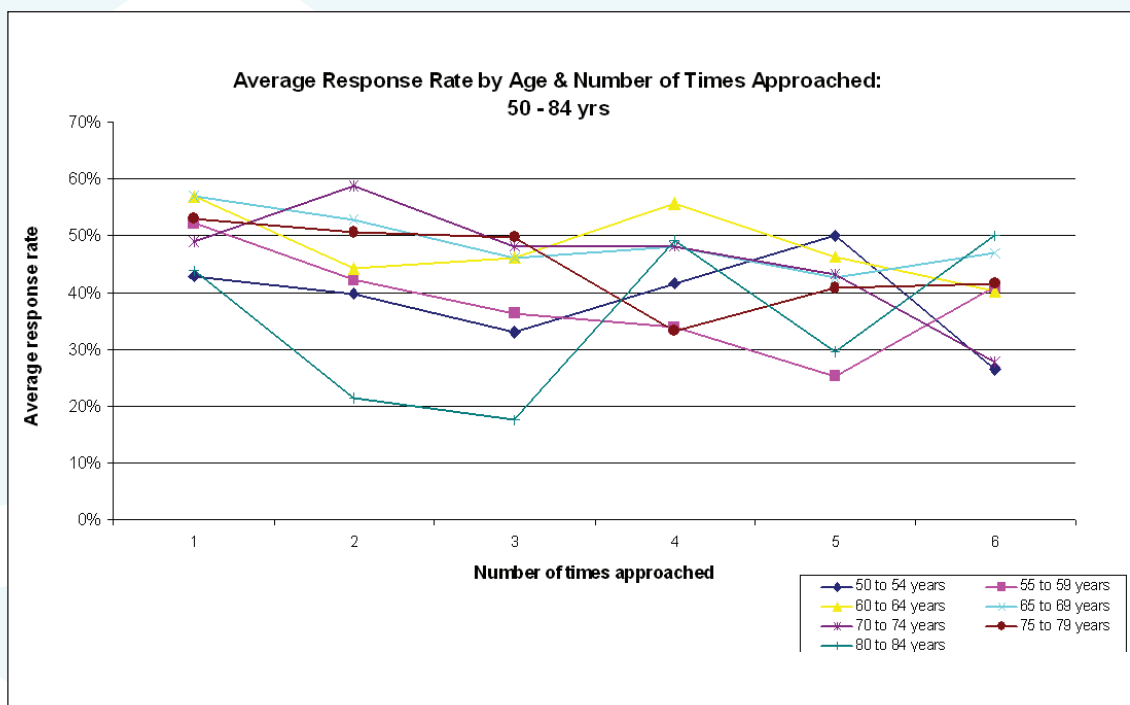




PARTICIPATION

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Graph 6:
Positive Response Rates by Age and Number of Times Approached: Senior Members 50 – 84 years old



These results suggest that in order to maximise response, twins who have been approached less than three times over the past 10 years should be given priority in sorting for study approaches and that new recruitment to the ATR may be best directed towards the specific age groups relevant to study needs.

REIMBURSEMENT AND INCENTIVE

The ATR does not offer reimbursement to participants for the costs of participating in a study – this issue is the responsibility of the researcher and is dictated by the funding and resources available. Any proposal to offer reimbursement is requested as part of the ATR Application form and is also subject to local institutional Ethics Approval. Generally, reimbursement for travel expenses is offered to participants who are asked to travel to a location to participate in the

research project. Reply Paid envelopes are provided for any material to be mailed back to the ATR or researcher, and the provision of a 1800 number is encouraged to minimise telephone costs to the participant should they wish to contact the researcher directly.

Individual members usually derive little or no additional benefit from participating in studies beyond the awareness of their valued contribution to medical and social research. Many studies, however, do have direct benefit to twins as a group as they focus on study of health and social issues related to being a twin, or to twin pregnancy and birth.

In some situations, a researcher may offer a financial or in kind incentive to members to encourage participation in a study. These proposals are considered carefully during the application process to assess reasonableness and are also subject to review by the institutional HREC. In controlled trials, the participating member may be provided with supplements such as vitamins. In placebo control trials, the ATR encourages researchers to offer the equivalent incentive to the placebo control twin at the conclusion of the trial. In rare cases, participants are offered incentives, such as vouchers to major shopping centres.

BENEFITS OF PARTICIPATING

Twins may also derive associated benefits as a by-product of participation in the study, such as detailed health information not normally available (MRI, bone density measurements). They may also be provided with the results of zygosity testing. The results of these tests may in some instances, and with the written consent of the member, be forwarded to the member's preferred medical practitioner.

Twins are only to be informed of the results of these tests if they have agreed to receive them and understand what they will receive, and where services or referral options are provided by the researcher to answer any concerns that may arise. This is particularly important if disease status or genetic testing results (other than zygosity) are provided. Under no circumstances will results of a twin be provided to a co-twin unless written consent has been given by the individual. Twins may also make a specific written request to the researcher for any test results pertaining to them if they participate in a study.

RECOVERY OF EXPENSES

The Australian Twin Registry (ATR) charges researchers for the cost of mailing out and follow up of potential study participants. In 2007, the ATR revised its fee structure for use of the facility. These prices are updated when postage, material or labour costs change.

Recovery of Expenses

The ATR charges researchers for the cost of mailing out and follow up of potential study participants. In 2007, the ATR revised its fee structure for use of the facility.

Set Up and Administration Fees

A one-off set up fee of \$150 - \$250 is charged, the amount depending on the logistics and complexity of the study. This covers set up of the study on the ATR database and general administration required to begin recruitment.

Mail Out Costs

Administration associated with mailouts is charged at 3 hours per 100 approaches at \$35.00 per hour. This charge covers labour required to select potential participants, create database mailout files, print, photocopy, collate, fold and insert approach documentation and sort ready for bulk mailing. Mailout materials and postage are charged on a cost recovery basis. For a Standard mailout of 100 letters, the cost of mailout materials, postage and administration is approximately \$200.

Reply Paid

Researchers are charged the cost of Reply Paid postage, which is calculated based on the total mailed response rate and averages \$25 - \$75 per 100 letters sent (based on a 25 - 75% response rate at \$0.50 per mail piece received).

Response Processing

Researchers are charged for the administration time required to process responses to their mailout. This task includes opening and sorting mail related to the study, logging the ATR member's response, entering any special requirements defined by the member (i.e. specific times to contact, interest in participation in specific phases of the study) and filing ready for end of week reporting. This is charged at the administration rate of \$35.00 per hour. Time taken to complete this activity per study is logged in the ATR database, which allows detailed invoices to be generated for researchers.



PARTICIPATION

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Follow Up Letters

Depending on the researcher's requirements, Follow Up letters may be used to prompt those ATR members who do not respond to the initial mailout. Follow Up letters are charged as above, and costs for this largely depend on the initial total response rate and the researchers own timeframes and requirements.

Follow Up Phone Calls

This service is optional for researchers and use depends on the researchers own timeframes and requirements. Phone follow up costs are calculated at \$48.50 per hour as a rolled up rate for labour, line and call costs. The number of hours required depends on how soon researchers wish phone follow up to occur (before or after a follow up letter etc) and whether the study is eligible for verbal consent to be taken. Again, time taken to complete this activity is logged on the ATR database for invoicing purposes.

Reporting

Researchers are charged for the administration time required to report on ATR members interested in participating in their study. This activity covers end of week quality checks, generation of response rate reports and uploading electronic files to researchers. This task usually takes half an hour to an hour per week per study depending on the complexity and scale of the study and is charged at the administration rate of \$35.00 per hour. Time taken to complete this activity per study is logged for invoicing purposes.

Tracing and Resending

Costs for tracing and re-mailing of any Return To Sender letters are borne by the ATR.

A typical Standard Approach including Set Up, Approach, Admin, Reply Paid and Phone Follow Up costs approximately \$620 per 100 letters (50 Adult pairs or 50 Junior families). This will generally return a response of between 30 – 60% depending on the study topic and participant burden.

CONFIDENTIALITY

If names and addresses of twins are released by the ATR in confidence to a researcher, he or she must guarantee that the information will be used only in accordance with the protocol approved by the ATR. In particular, no confidential information (including names and addresses) may be passed on to any third party without written approval from the ATR, in addition to HREC approval.

The ATR does not provide:

- complete anonymity of participants (i.e., researchers will know the identity of participants)
- participants with the option of being identified in any publication arising from the research
- for participants to be referred to by pseudonym in any publication arising from the research
- personal information obtained from a Commonwealth Department or Agency

ADVERSE EFFECTS AND COMPLAINTS

The ATR takes any complaint from members seriously and endeavours to promptly resolve the issue presented

The ATR requires all adverse effects and complaints to be communicated to ATR Management.

There were no adverse effects or formal complaints communicated to the ATR in the period July 2006 – June 2007.

While the ATR is not an agency for the welfare of twins, it is inevitably contacted by twins and their friends and family members who are seeking help with specific issues, which may or may not have been raised as a result of an invitation to participate in a study. The ATR retains contact details for various individuals and organisations (such as psychiatrists, psychologists, bereavement counsellors, twin groups, researchers) that are capable and willing to offer assistance with particular questions or problems. If possible and appropriate, ATR staff can suggest one or more of these organisations to the enquirer.

VALUE-ADD

Development of projects and programs to value-add to twin research in Australia

ATR RESEARCH ARCHIVE

The ATR is establishing a consolidated electronic archive of data compiled from completed and ongoing ATR studies. This research archive is anticipated to address specific issues such as reducing duplication of data collection from twins, and provide a mechanism for the ATR to establish communication between researchers with similar study topics or data collection plans. Access will be available to all Australian researchers and their collaborators under ATR guidelines and any conditions stipulated by the contributing researcher regarding third party access to their data.

In 2006, Professor Margaret Otlowski, a member of our ATR Advisory Board and Professor of Law at the University of Tasmania, established a small sub-committee comprising researchers interested in the activity. The recommendations of the sub-committee were that the archiving project requires specific expertise, time and project management, including the development of a detailed set of archiving parameters to assist in managing the data into the future. This work will allow the archive to begin with a solid foundation and enable it to grow to accommodate researchers and data from a range of areas. The sub-committee also recommended that the ATR seek specific skills and assistance to make this project a success.

The ATR has baseline demographic and general health data, collected in 1982, 1984-92, and 1997 which will form the basis of a pilot project investigating the various needs and issues surrounding the archive's development. It is anticipated that this pilot study will be completed in 2008.

ATR BIOBANK

The ATR plans to establish a backed-up Biobank of DNA samples and other biospecimens collected from previous twin studies, and a central inventory of existing biospecimens stored in other laboratories. As with the ATR research archive, access to the repository will be available to all Australian researchers and their collaborators under ATR guidelines. It is envisaged that the Biobank will facilitate future research and collaborations without the need to request and collect additional biospecimens from ATR members. Work on the set-up and development of the biorepository will follow the establishment of the data archive as core issues such as access, consent and coordination will be similar for both resources. However, when the ATR's central database was recently overhauled, the capacity to link an ATR member record with information on any of their stored biospecimens was included.

In the future, numerous studies including low-cost, modest projects could be supported via access to these national research resources without adding to the burden of participation for ATR members.



GOVERNANCE

Governance of the ATR in a fair, transparent and equitable manner

ATR MANAGEMENT

As at end June 2007, the ATR Management comprises:

- Prof. John Hopper, Director, Australian Twin Registry, NHMRC Senior Principal Research Fellow, Director (Research), Centre for Molecular, Environmental, Genetic and Analytic (MEGA) Epidemiology
- Dr Susan Treloar, Deputy Director, Australian Twin Registry, Population Studies and Human Genetics Division, Queensland Institute of Medical Research
- Prof. Nicholas de Klerk, Director, Western Australia Twin Child Health (WATCH)
- Dr Ruth Morley, Director, mothers and their twin children (match)
- Prof. Lyle Palmer, Director, Western Australian Twin Register (WATR)
- Mr Vincent Pollaers, Chair, Advisory Board
- Emily England, ATR Co-ordinator
- Jenny Boadle, ATR Project Support Officer
- Kim Dorrell, ATR Senior Project Officer (maternity leave until second half of 2007)

Any member of ATR Management with a potential conflict of interest is required to declare this interest prior to any relevant discussions. Persons with a conflict of interest in any study are excluded from review or application approval processes of that study. Members of the Advisory Committee are available to help act as independent reviewers. In the event that the Director or Deputy Director is involved in a study as a researcher, they take no part in the approval process. If both are involved or unavailable, an independent person is brought in to oversee the processing of the application.

ADVISORY BOARD AND CHARTER

The ATR Advisory Board was constituted and met for the first time on 14th October 2005. The Advisory Board met again on the 29th May 2006, with the next meeting scheduled for October, 2007.

Enabling Grant Goal: Establish an active and effective Advisory Board

An Advisory Board Charter was developed and approved by the Advisory Board in June 2006, which clearly states its terms of reference and governs its involvement in the ATR.

As at June 2007, the current members of the Advisory Board are:

- Professor Annette Dobson (University of Queensland)
- Dr Paul Jelfs (Child Support Agency, ACT)
- Professor Peter Klinken (Western Australia Institute of Medical Research)
- A/Professor Paul Lancaster (University of Sydney)
- Professor Margaret Otlowski (University of Tasmania)
- Mr Vincent Pollaers (Twin Representative, Chair, New South Wales)
- William Mackerras (Twin Representative, Australian Capital Territory)
- Vacant (Australian Multiple Birth Association (AMBA) Representative)

Ex-officio:

- Professor John Hopper (Director, ATR, University of Melbourne, Victoria)
- Dr Susan Treloar (Deputy Director, ATR, Queensland Institute of Medical Research)

DISPUTE RESOLUTION PROCESS

An important task for the new Advisory Board was to establish a Dispute Resolution Process to enable impartial and transparent management of any dispute arising between the ATR and stakeholders. A document describing the Dispute Resolution Process was approved by the Advisory Board in August 2006.

EXPERT REFERENCE GROUP

The ATR convened an Expert Reference Group (ERG) in August 2006. The ERG operates under a Charter, developed by ATR Management and the Advisory Board. The Charter describes the ERG's role and responsibilities in supporting the transformation and growth of the ATR and to enhance the ATR's service levels and support to the research community. During the preparation of this Charter, the Advisory Board took into consideration the ATR's vision; commitments made in the Enabling Grant; current and future needs of the ATR; past correspondence; recent comments from members of the Executive Committee and; past Minutes of Executive Committee meetings.

Members of the ERG are:

- Professor Sam Berkovic, Epilepsy Research Centre, Austin Hospital, Melbourne, Victoria
- Professor Brian Byrne, School of Psychology and Language and Cognition Research Centre, The University of New England, New South Wales
- Professor Nick de Klerk, Department of Biostatistics & Genetic Epidemiology, Telethon Institute for Child Health Research, Western Australia
- Dr Ruth Morley, Department of Paediatrics, Royal Children's Hospital, Melbourne, Victoria

- Professor Lyle Palmer, Laboratory for Genetic Epidemiology, Western Australia Institute of Medical Research, Western Australia
- Dr Claire Roberts, Obstetrics and Gynaecology, The University of Adelaide, South Australia
- Dr Melissa Southey, Genetic Epidemiology Laboratory, Department of Pathology, University of Melbourne, Victoria
- Professor John Wark, Department of Medicine, Royal Melbourne Hospital, Victoria

Ex-officio:

- Professor John Hopper (Director, ATR, University of Melbourne, Victoria)
- Dr Susan Treloar (Deputy Director, ATR, Queensland Institute of Medical Research)

The ERG is not a policy making body, nor is it intended to be a user representative body, rather it is a resource available to the ATR to proactively and positively assist it in pursuing the ATR's primary objectives. Membership is reviewed on an annual basis in line with developing the energy, vision and commitment of the next generation of researchers to the work of the ATR.



GOVERNANCE

Governance of the ATR in a fair, transparent and equitable manner

CONSUMER REPRESENTATION



Vincent Pollaers

The ATR Advisory Board is chaired by twin representative Vincent Pollaers. Vince, and his twin brother John, are long term members of the ATR and have participated in studies dating back more than 25 years. Vince brings a wealth of experience, energy, interest and expertise to the ATR.

In previous roles, Vince has been responsible for developing and managing alliances between IBM and third party companies throughout Asia Pacific. Prior to this, he was Strategy Executive for IBM Global Services in Australia /New Zealand and was responsible for providing advice and guidance on initiatives which would shape the future direction of the company's business model and services and products portfolio. Vince joined IBM in 2001 and for four years held the position of General Counsel of IBM Australia & New Zealand, managing a team of 17 lawyers and providing legal support to all of IBM's business units in the region. Vince has also held positions as a solicitor in a number of internationally recognised law firms, as an IT marketing consultant with Price Waterhouse in Hong Kong, and as a Weapons Electrical Engineering Officer in the Royal Australian Navy. He holds Bachelors' degrees in Electrical Engineering and Computing Science, and is admitted as a solicitor in Australia, England and Wales. Vince is very interested in the areas of organisational development and culture and is currently undertaking a post graduate diploma in counselling and psychotherapy.



William Mackerras

William Mackerras is also a twin representative on the Advisory Board, having taken this position over from his twin brother, Patrick in early 2006, and before that their father, Malcolm Mackerras, AO, the well-known political commentator, twin and member of the ATR.



Ann Marie (pictured at front) with her family

Ann Marie Harli is a mum of twins, and is currently serving on the ATR Advisory Board as the representative of the Australian Multiple Birth Association (AMBA). Ann Marie is the current Chair of the AMBA National Board and has been active in AMBA since the birth of her twins Grace and Amber, now aged 13.



Dr Sue Treloar

The ATR's Deputy Director, Dr Sue Treloar is also a twin, and long term member of the ATR.

Sue is pictured below, with her twin sister Caroline. Sue and Caroline were 18 when this picture was taken, having just received identical passes in their Higher School Certificate exams.

Sue and Caroline participated in the Canberra questionnaire study in 1980 (Gibson, Matthews and Martin) before moving several times and away from Sydney. For a time they were "lost" members, until Sue met Nick Martin in QLD in 1986. Nick reminded Sue to contact the ATR to update her address.

Sue became involved in twin studies, completing a PhD on women's gynaecology and mental health issues in 1993. The study collected data from 1600 ATR female twin pairs. Sue is now a respected researcher in the area of women's health including the genetics of endometriosis and age at menopause.



Sue and Caroline Treloar

ATR STAFF

The ATR is administered through the University of Melbourne, within the Centre for Molecular, Environmental, Genetic and Analytic (MEGA) Epidemiology, in the School of Population Health. The ATR currently employs 2 full time (Coordinator and Project Support Officer) and 1 part time (Senior Project Officer) Administration staff, 5 casual Research Assistants (hours cumulated to a total 2.25 EFT) and a part time Database Manager. The ATR also provides an honorarium towards a part time Deputy Director.

Core ATR Staff as at June '07:



*Professor
John Hopper
Director*



*Dr **Susan Treloar**
Deputy Director*



***Kim Dorrell**
Coordinator
(to July 06)
Senior Project
Officer
(from July 07)*



***Emily England**
Coordinator
(from July 06)*



***Jenny Boadle**
Project Support
Officer*



***Marian Fenwick**
Research Assistant*



***Helen Rodais**
Research Assistant*



***Shaie O'Brien**
Research Assistant*



***Jackie Arbuckle**
Research Assistant*



***Susan McKenna**
Research Assistant*

***Kelly Aujard**
Database Manager*

***Maggie Angelakos**
Assistant Data Manager*

Administration and Assistant staff are employed via (and subject to terms and conditions of) the University of Melbourne. The part time Deputy Director position is occupied by an external Researcher, employed via their local institution. The ATR provides an honorarium via invoice from the researcher's institution.

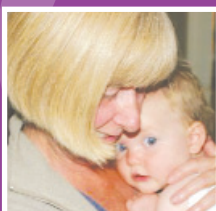


GOVERNANCE

Governance of the ATR in a fair, transparent and equitable manner

ATR (match) STAFF

match is currently administered through the University of Melbourne, Department of Paediatric and supported by the Murdoch Children's Research Institute



Dr Ruth Morley (with grandchild Iona) – match Director



Dr Supriya Raj – match co-ordinator

ATR (WATR) STAFF



Professor Lyle Palmer, WATR Co-Director



Jessica Lee, WATR Co-ordinator

ATR (WATCH) STAFF



Nick De Klerk – WATCH Director



Jan Hansen – WATCH Coordinator



Phyllis Alessandri – WATCH Research Assistant

STAKEHOLDER SURVEY

In 2005, the ATR Advisory Board launched a consultation process intended to gather information on perceptions and experiences of the users of the ATR's facilities, and to advise on how the ATR might improve the services it provides. As part of this information gathering exercise, the Advisory Board recommended that ATR Management commission an independent survey of past and present users of the ATR.

In September 2006, a Feedback Questionnaire was sent to each researcher and primary research staff who had used the ATR's facilities for specific projects in the past 5 years. The questionnaires were collated and data analysed by an independent company, Venus Research, which specialises in customer satisfaction research. Respondents were asked to provide detailed and frank responses to help the ATR move forward and improve its services to the research community.

The study respondents were typically of senior status with almost half (46.8%) either Principal or Chief Investigator. Almost three quarters of respondents (72.3%) communicated with the ATR by email, with well over half (57.4%) communicating by phone. Communication/contact with the ATR was rated highly overall, with the mean score of all ratings at 5.2/6.0. The overall value of the ATR's contribution to client work was rated 5.1/6.0 (overall mean), and the value of the feedback received from the ATR and the application process itself was 4.7/6.0 (overall mean).

An area identified for improvement was the level of twin response to participation in studies, which was rated at 3.9/6.0. Verbatim comments indicated that a more astute and knowledgeable follow up of twins approached for each study could potentially increase this response level.

Researchers were asked to consider methods to manage the demand on twins for participation in studies, and suggestions included offering incentives and "collaboration and cooperation" between the various studies. The ATR's annual newsletter and Community Updates by email were the activities that respondents rated as of highest interest at 5.2 and 5.1/6.0 respectively.

There was a high level of interest for a research archive rated at 5.3/6.0. The level of interest in a bio-repository for DNA and biospecimen storage was also high, with over a quarter of respondents (25.6%) who gave a rating, registering their interest in it as 6/6.

The summary report for the survey is available at: http://www.twins.org.au/files/Stakeholder_Survey_Report.pdf

In future, at the end of each project, the ATR intends to ask the researchers involved to complete a similar questionnaire so that the ATR may learn from each project. Likewise, plans are underway to survey twin volunteers to gauge their experiences.

ATR BUDGET

The ATR welcomes donations towards the administration and management of the ATR. Donors are provided with a receipt for their donation. Donations may be earmarked for specific activity.

Commercial partnerships that involve in kind or financial incentive for the ATR may be entered into after approval by the ATR Management and Advisory Board. Under no circumstances shall a commercial partnership undermine or bias the impartiality and transparency of the ATR. Commercial partnerships resulting via researcher projects will not confer advantage or additional ATR support to that project beyond that offered to all other researchers.

The NHMRC Enabling Grant Special Facilities Scheme provides the ATR with a budget of \$350,000 per annum. The funding period extends from 1 July 2004 to 30 June 2009 for a total of 5 years. In addition, the ATR recovers costs associated with approaching twins for studies from researchers.

The funding level provided by the Enabling Grant represents 70% of funds requested in the ATR's Enabling Grant Special Facilities Scheme grant application, which contained a budget framework of \$500,000 per annum. The funding request incorporated costs for WATCH and match, the Research Travel Grant Scheme and new developments including the Biorepository and Data Archive. Given the reduced funding granted, it is unlikely that the ATR will achieve all of the milestones indicated in the grant application within the current 5 year span.

The following Financial Statement outlines the Actual and Proposed budget for 2005 – 2009. It is evident that during the latter part of the Enabling Grant period, the ATR will need to seek bridging funds from an alternative source to maintain current momentum and service levels. In addition, a review of researcher charges will be undertaken to ensure that reasonable costs are being recouped.



2007 FINANCIAL STATEMENT

	2004 Actual	2005 Actual	2006 Actual	2007 Proposed	2008 Proposed	2009 Proposed
Income/Credits						(1/2 Year Only)
NHMRC	252,057	350,000	350,000	350,000	350,000	175,000
Costs Recouped from Researchers	41,633	13,727	43,213	49,258	60,000	25,000
Other Costs Recouped (Registration Fees etc)				67,384		
Total Income/Credits	293,690	363,727	393,213	466,642	410,000	200,000
Refunds				6,923.07		
Balance brought forward from previous year	68,992	103,010	21,503	1795	-24,262	-13,648
Researcher debt write-off	-1,293					
Total funds	361,389	466,737	21,503	475,361	385,738	186,352
Expenditure						
Permanent Salaries (including on-costs)	111,291	112,888	144,111	154,403	155,000	77,500
Casual Salaries	24,679	34,577	68,331	131,000	112,000	55,000
		78,156				
Subtotal salaries	135,970	225,622	212,442	285,403	267,000	132,500
Other Expenditure						
Contracted Services Fees	26,788	32,573	35,964	44,232	2,000	
Consumable Supplies	595	121	80	294	500	250
Stationery	2,007	2,741	3,054	4,529	5,000	2000
Travel, Accommodation & Conference Registrations (including <i>It Runs in the Family</i>) & Travel Grants	9,782	19,878	26,432	36,020	6,000	1000
Entertainment	1,798	1,233	2,363	272		
Postage	20,339	24,153	25,799	22,970	6,000	3000
Telephones - 1800 Freecall number, STD and Local	3,034	6,575	6,854	7,997	8,000	4000
Software Licensing	3,370	3,454	3,540	3,540	3,540	
Equipment Purchase & Maintenance	6,239	2,147	5,346	3,217	500	75
Internal Computing Charges (Website Hosting etc)	587	622	486	500	500	500
Photocopying (Internal)	1,157		11			
Copying (Design & Print Centre – Mailout Materials)	11,324	1,896	120	208	500	100
Printing (Design & Print Centre – Newsletter/Annual Report)	13,450	16,591	21,204	4,000	15,000	
Advertising	745		2,989	1,559		504
Journal Subscriptions	212	357	323			
Freight/Couriers	105	225	535	35		
Parking	32	18	8			
Staff Training and Development	370	235				
Subtotal Other Expenditure	101,934	112,819	136,108	129,373	47,540	11,429
WATCH						
Salaries						
Project Co-ordinator 0.4 FTE, ICHR SRO 2 – Jan Hansen	7,455	14,910	14,910			
Research Clerk 0.6 FTE, ICHR RSC 6 – Kerry Coleman	8,977	17,954	17,954			
Other Expenditure						
Postage (including reply paid)						
Initial letter: 315*\$4						
Follow up letters: 200*\$2						
Resending questionnaires 50*\$2						
Printing 500*\$10						
Stationery (envelopes etc.)						
Telephone calls 1500*\$1						
Data entry (questionnaire development, scanning etc)						
Computer maintenance etc						
Subtotal of Other Expenditure	5,516	11,032	11,032			
Subtotal WATCH	-	65,844	43,896	43,896	43,896	21,948
MATCH						
Salaries – Cohort Co-ordinator 0.5 FTE		40,950				
Other Expenditure eg. recruitment kit, planning meetings	20,475					
Subtotal MATCH	20,475	40,950	20,475	40,950	40,950	20,475
Total Expenditure	258,379	445,235	412,921	499,622	399,386	186,352
Balance as at 31st December						
(Total Funds – Total Expenditure)	103,010	21,502	1,795	-24,262	-13,648	0

APPENDIX 1

Full List of Approved ATR Studies

Study No.	Researchers and Study Title	Time Frame	Page
00-001	Prof John Eisman (Garvan Institute Of Medical Research) Professor John Eisman (Garvan Institute, Sydney) OESTROGEN AND VITAMIN D INTERVENTION STUDY	COMPLETED	—
81-001	Prof Grant Townsend (The University Of Adelaide) Professor Brown, Dr Richards, Mr Travan (University of Adelaide) Teeth and Faces of Young Australian Twins	1981-2005 ACTIVE – ONGOING PROGRAM	44
84-001	Prof John Eisman (Garvan Institute Of Medical Research) Osteoporosis	1984- COMPLETED	—
87-001	Prof Sam Berkovic (Epilepsy Research Centre) Epilepsy in Twins	1987- COMPLETED	—
88-001	Prof John Hopper (MEGA Epidemiology) Professor Margaret Hamilton (University of Melbourne), Dr David Hill, and Ms Vickie White (Anti-Cancer Council of Victoria) Longitudinal study of adolescent and young adult twins	1988- COMPLETED	—
88-001-2	Prof John Hopper (MEGA Epidemiology) Professor Margaret Hamilton (University of Melbourne), Dr David Hill, and Ms Vickie White (Anti-Cancer Council of Victoria) Longitudinal study of adolescent and young adult twins: Phase II	1988-2002 COMPLETED	—
88-001-3	Dr Vicki White (The Cancer Council Of Victoria) Why one twin smokes and the other doesn't: Understanding the reasons why children growing up in the same family develop different smoking behaviours (YATS Smoking Study)	2002- COMPLETED	—
88-001-4	Dr Vicki White (The Cancer Council Of Victoria) Genetic and environmental determinants of tobacco and alcohol use trajectories into adulthood: a prospective twin study (YATS Tobacco & Alcohol)	2003- ACTIVE – DATA ANALYSIS	51
88-002	Prof John Hopper (MEGA Epidemiology) Ego Seeman Co-twin Control Study of Tobacco Use and Bone Mass (Twins)	COMPLETED	—
89-001	Prof John Hopper (MEGA Epidemiology) Ego Seeman Twin-family study of lifestyle, genetic and environmental causes of variation in bone mass (A Study of Bone Mass in Twins and Their Families)	COMPLETED	—
90-001	Prof John Wark (The University Of Melbourne) Prof John Hopper (University of Melbourne), Prof Caryl Nowson (Deakin University), Prof Richard Larkins, Prof Doris Young (University of Melbourne) DIETARY INTERVENTIONS AND BONE MASS: PROSPECTIVE STUDIES IN FEMALE TWINS [Factors in gain and loss of bone in young, menopausal, and elderly twins] (Royal Melbourne Twin Bone Study, Royal Melbourne Twin Research Program, Twin and Sister Bone Research Program)	1990- ON HOLD	48
90-001-2	Prof John Wark (The University Of Melbourne) Prof John Hopper (University of Melbourne), Prof Caryl Nowson (Deakin University), Prof Richard Larkins, Prof Doris Young (University of Melbourne) The effect of long-term calcium supplementation on bone densitometry in young female twins (an extension of the Twins Bone Program) (Royal Melbourne Twin Research Program)	1991- ON HOLD	48
91-001	Prof Tony Cunningham (Westmead Hospital) Dr Hassan Naif (Westmead Hospital) Host cell genetic effect on HIV-1 replication in monocytes and macrophages using identical and non-identical twins	1991-2001 COMPLETED	—
91-002	Prof Stephen Harrap (The University Of Melbourne) Prevention of coronary disease – A genetic approach "The Victorian Family Heart Study" (VICTORIAN FAMILY HEART STUDY)	1991-2006 ACTIVE – DATA ANALYSIS	31
91-002-2	Prof Stephen Harrap (The University Of Melbourne) The Family Study of Heart Size	1997-2000 ACTIVE – DATA ANALYSIS	31
91-002-3	Prof Stephen Harrap (The University Of Melbourne) Dr Shannon Harrison, Dr Rodney Sinclair, Dr Justine Ellis, The Prevention of Coronary Disease – A Genetic Approach: The Androgen Receptor and Female Androgenetic Alopecia (Vic Family Heart Study – Female Baldness Control Study)	2002- ACTIVE – DATA ANALYSIS	31



APPENDIX 1

Full List of Approved ATR Studies

Study No.	Researchers and Study Title	Time Frame	Page
92-001	Prof Patricia Noller (The University Of Queensland) Candida Peterson, Grania Sheehan (University of Queensland) SIBLING PERCEPTIONS OF DIFFERENTIAL PARENTAL TREATMENT	1992- COMPLETED	—
92-002	Mr Greg Murray (The University Of Melbourne) Survey Study of Seasonality	1992- COMPLETED	—
92-003	A/Prof Ego Seeman (Austin & Repatriation Medical Centre) Tobacco consumption, peak bone density and body composition in children: a co-twin control study (Smoking and Bone Mass, Adol. Smoking)	1992- COMPLETED	—
92-008	Dr Sue Treloar (Queensland Institute Of Medical Research) Menopause, hysterectomy, and HRT: genetic and environmental influences (Menopause Study)	1991- COMPLETED	—
92-011	Dr Edward McMurchie (CSIRO) Dr Caryl Nowson (Deakin University) Genetic Factors associated with altered cheek cell sodium transport in human hypertension: a twin study (HUMAN CHEEK CELLS, SODIUM TRANSPORT AND ESSENTIAL HYPERTENSION)	1992-1997 COMPLETED	—
93-001	Prof Brian Morris (Institute For Biomedical Research) Molecular genetics of essential hypertension	1993-1999 COMPLETED	—
93-005	Prof Nick Martin (Queensland Institute Of Medical Research) OVER 50s TWIN STUDY: PSYCHOLOGICAL PREDICTORS OF DISEASE OUTCOMES (Over 50s Twin Study)	1999 COMPLETED	—
93-007	Dr Judith Burstyner A study of dental anxiety and psychological variable in female twins (DENTAL ANXIETY IN FEMALE TWINS)	1993-1998 COMPLETED	—
93-011	Prof Nick Martin (Queensland Institute Of Medical Research) Dr Adele Green, Dr Joanne Aitken (QIMR) LONGITUDINAL STUDY OF MELANOCYTIC NAEVI IN TWINS (Mole Development in Pubescent Twins) (Twin Mole Study)	1993-2008 ACTIVE – ONGOING PROGRAM	38
93-014	Prof Patricia Noller (The University Of Queensland) A/Prof Candida Peterson, Dr Judith Feeney Sibling perceptions of differential treatment by parents: Outcomes for personality, social competence and health	1993- COMPLETED	—
93-015	A/Prof Florence Levy (The Prince Of Wales Children's Hospital) Professor David Hay (Curtin University of Technology) Attention Deficit Hyperactivity Disorder in Twins and Siblings (Australian Twin ADHD Study)	1993-2002 COMPLETED	—
93-016	Prof Nancy Segal (California State University At Fullerton) Twin Study of Bereavement	1993-1997 COMPLETED	—
94-004	A/Prof Tracey Wade (Flinders University Of South Australia) Investigating the genetic epidemiology of disordered eating (TWIN STUDY OF EATING PATTERNS)	1994-1997 COMPLETED	—
94-005	Prof John Hopper (MEGA Epidemiology) Prof Graham Giles (ACCV), Dr Margaret McCredie (NSW Cancer Council), Dr Dallas English (ACCV), Dr Norman Boyd (Ontario Cancer Institute), Dr Martin Yaffe (Sunnybrook Hospital, Toronto, Canada) A twin study of mammographic breast density and the risk of breast cancer (A TWIN STUDY OF MAMMOGRAPHIC PARENCHYMAL PATTERNS AND BREAST DENSITY)	1994-2003 ACTIVE – ONGOING PROGRAM	35
94-005-2	Prof John Hopper (MEGA Epidemiology) Genetic and Environmental determinants of mammographic density: A twins and sisters study (The Australian Twins and Sisters Breast Density Study)	2003-2012 ACTIVE – ONGOING PROGRAM	35
94-007	Dr Leon Flicker (The University Of Melbourne) Prof John Wark, Prof John Hopper (University of Melbourne) Bone Density in Elderly Female Twins	1994-2002 COMPLETED	—
94-008	Ms Katie Wood (Swinburne University Of Technology) Professor David Hay (Curtin University of Technology) Attention deficit disorder with and without hyperactivity	1994-1999 COMPLETED	—

Study No.	Researchers and Study Title	Time Frame	Page
94-099	Dr Colin Robertson Prof Peter D Phelan (Royal Melbourne Children's Hospital) Asthma, atopy and bronchial reactivity in twins	1994-1995 COMPLETED	—
95-002	Prof Philip Sambrook (Royal North Shore Hospital) Genetics of cervical and lumbar spondylosis	1995-1996 COMPLETED	—
95-004	Prof Nick Martin (Queensland Institute Of Medical Research) Dr John Whitfield (RPA Hospital), Dr Andrew Heath (St Louis, USA) Persistence and change in drinking habits: A twin-family study (Twin Alcohol Study)	1995-2002 ACTIVE – DATA ANALYSIS	38
96-001	A/Prof Ego Seeman (Austin & Repatriation Medical Centre) Ms Georgina Pearce, Mr Yung Van Ho, Ms Sheila Matthews (Austin & Repatriation Hospital) BONE MASS IN ADOLESCENT MALE-MALE AND MALE-FEMALE TWIN PAIRS	1996- ACTIVE – ONGOING PROGRAM	43
96-002	Dr Raymond Kelly (St Vincent's Hospital/VCCRI) Dr Chris Hayward (St Vincent's Hospital) Non-invasive assessment of genetic influences on cardiovascular function	1996-1999 COMPLETED	—
96-003	Dr Michael Nicholls (The University Of Melbourne) The effect of uterine hormonal levels upon lateral preference	1996-1998 COMPLETED	48
96-005	Prof John Wark (The University Of Melbourne) Prof John Hopper (University of Melbourne), Dr Simon Foote (WEHI) Risk genes for osteoporosis and other common diseases: a twin approach to interval mapping of loci (an extension of the Royal Melbourne Twin Bone Research Program) (Royal Melbourne Twin Bone Study, Royal Melbourne Twin Research Program)	1996- ON HOLD	—
96-005-1	Prof John Wark (The University Of Melbourne) Prof John Hopper (University of Melbourne), Dr Simon Foote (WEHI) Protocol amendments: Fasting blood sample and Genetics of Common Human disease – a twin study (Gemini Genomics AUS002) (Twin Bone Study – Gemini Protocol AUS002)	1996- ON HOLD	—
96-006	Prof Nick Martin (Queensland Institute Of Medical Research) Dr Paul Burton, Prof John Hopper, Dr Mark Jenkins (University of Melbourne), Prof David Hay (Curtin University of Technology) An Australian multi-centre twin-based study of the genetic epidemiology of asthma and atopy	1996-1999 COMPLETED	46
96-007	Dr Sue Treloar (Queensland Institute Of Medical Research) Genetic epidemiology of endometriosis	1996-2010 ACTIVE – WRITING UP	46
96-007-2	Dr Sue Treloar (Queensland Institute Of Medical Research) Genes Behind Endometriosis	1999-2010 ACTIVE – WRITING UP	46
96-007-3	Dr Sue Treloar (Queensland Institute Of Medical Research) Dr D Purdie, Prof Adele Green, T Bell Antenatal, childhood and adolescent risk factors for endometriosis (Risk Factors for Endometriosis)	2001-2010 ACTIVE – WRITING UP	46
96-008	Dr Sue Treloar (Queensland Institute Of Medical Research) Twin studies of pre-eclampsia/eclampsia	1996- COMPLETED	—
96-009	Prof Philip Sambrook (Royal North Shore Hospital) Twin Studies of the genetics of osteoarthritis and osteoporosis	1996-2008 ACTIVE – ONGOING PROGRAM	32
96-010	Dr Margie Wright (Queensland Institute Of Medical Research) Prof Nick Martin The genetic determinants of working memory, information processing and intelligence in twins (Quantitative & Molecular Genetic Analysis of Intelligence, Genes for cognition: The Brisbane Twin Memory, Attention, and Problem Solving (MAPS) Study)	1996-2008 ACTIVE – ONGOING PROGRAM	51



APPENDIX 1

Full List of Approved ATR Studies

Study No.	Researchers and Study Title	Time Frame	Page
97-001	Prof Sam Berkovic (Epilepsy Research Centre) Epilepsy in Twins and Families: Analysis of Acquired Factors (CAUSES OF EPILEPSY)	1997-2002 COMPLETED	—
97-001-2	Prof Sam Berkovic (Epilepsy Research Centre) Prof Roger Short (Perinatal Research Centre, Royal Women's Hospital) Study of Twin Zygosity	1999-2001 COMPLETED	—
97-001-3	Prof Sam Berkovic (Epilepsy Research Centre) Dr Regula Briellman, A/Prof David Reutens, A/Prof Graeme Jackson Morphological and Spectroscopic Study of Monozygotic Twins Discordant for Epilepsy (Epilepsy and Twins Research Program; MRI Study)	2001-2010 ACTIVE – ONGOING PROGRAM	26
97-002	Prof Nick Martin (Queensland Institute Of Medical Research) Dr Kirsten Ohm Kyvik (Danish Twin Registry), Prof John Hopper (University of Melbourne) Diabetes in Australian Twins	1997-2002 COMPLETED	—
97-003	Prof David Handelsman (Concord Repatriation General Hospital) Epidemiology of Prostate Size in Healthy Australian Men	1997-2001 COMPLETED	—
97-004	Prof John Eisman (Garvan Institute Of Medical Research) Dr Chris White (Garvan Institute, Sydney) Genetic control of bone mineral density and ultrasound bone metabolism and body composition (an extension of Sambrook: "Genetics of cervical & lumbar spondylosis" (95-002) (Garvan Bone Study)	1997-1999 COMPLETED	—
97-006	Prof David Hay (Curtin University Of Technology) Prof Nick Martin (QIMR), Prof Florence Levy (Prince of Wales Hospital) Genetic relationship between adult behavioural traits and childhood behavioural disorders	1997-2002 COMPLETED	—
97-007	Dr Caryl Nowson (Deakin University) Predictors of blood pressure response to alterations in dietary salt	1997-2001 COMPLETED	—
98-001	Prof Brian Byrne (University Of New England) Genetics of Reading Ability	1998-2009 ACTIVE – ONGOING PROGRAM	27
98-002	Prof Con Stough (Swinburne University Of Technology) Mr John Song Brain Electrical Activity and Intelligence	1998-2002 COMPLETED	—
98-003	Prof Nick Martin (Queensland Institute Of Medical Research) Prof Wendy Slutske Familial transmission of antisociality / conduct disorder and alcoholism	1998-2002 COMPLETED	—
98-006	A/Prof Florence Levy (The Prince Of Wales Children's Hospital) Prof David Hay (Curtin University of Technology) A developmental/genetic approach to the determination and expression of ADHD	1998- ACTIVE – ONGOING PROGRAM See 2002-004-3	—
98-007	Prof John Wark (The University Of Melbourne) Dr Anne-Marie Cassano, Ms Natalie El Haber, Dr Kim Bennell A study of the heritability of balance in a cohort of twins (Gait and Balance Study)	1998-2006 ACTIVE – DATA ANALYSIS	49
98-008	Prof John Hopper (MEGA Epidemiology) Australian Breast Cancer Twin Family Study	1998-2010 ACTIVE – DATA ANALYSIS	34
99-001	Prof Patricia Noller (The University Of Queensland) Prof SRH Beach (University of Georgia) Understanding Twins in Situations of Comparison and Competition (Competition)	1999-2002 COMPLETED	41
2000-001	Dr Mark Mclean (Westmead Hospital) Dr Wah Cheung The relationship between birth weight and the Metabolic Syndrome: A study in twins	2000-2003 COMPLETED	—
2000-002	Prof Gordon Parker (Prince Of Wales Hospital) Genetically Driven Constructs of Temperament: Assessing Variation in Self-report Scales	2000-2005 ACTIVE – WRITING UP	42

Study No.	Researchers and Study Title	Time Frame	Page
2001–002	A/Prof Tracey Wade (Flinders University Of South Australia) How do interactions between genes and specific environmental risk factors cause eating disorders in women? (Variations in Eating Behaviour Among Women)	2001–2007 ACTIVE – DATA ANALYSIS	47
2001–003	Dr Janet Fletcher (The University Of Melbourne) Ms Deborah Loakes A Forensic Phonetic Investigation of the Voices of Identical and Non-identical Twins	2001–2002 COMPLETED	–
2001–004	Prof Nick Martin (Queensland Institute Of Medical Research) The Genetics of Vulnerability to Nicotine Addiction	2001–2006 ACTIVE – DATA ANALYSIS	39
2001–005	A/Prof David Mackey (Royal Victorian Eye & Ear Hospital) Dr Jamie E Craig, Dr Johan Poulsen, Dr James Morgan Twin study of ophthalmic screening parameters	2001–2008 ACTIVE – ONGOING PROGRAM	37
2002–002	A/Prof Bryan Mowry (Queensland Centre For Mental Health Research) Dr Domonique Hannah A Study of the Potential Causes of Psychosis in a Twin Sample	2002–2007 ACTIVE – ONGOING PROGRAM	41
2002–003	Prof Andrew Butcher (Flinders University) The Genetics of Voice: A Comparison of Acoustic Parameters in MZ and DZ Twins (Genetics of Voice)	2002– COMPLETED	–
2002–004	Prof David Hay (Curtin University Of Technology) A/Professor Florence Levy Genetic Comparison of two measures of Attention Deficit Hyperactivity Disorder (ADHD) (A Study on the Behaviour of Children in Families with Twins)	2002– COMPLETED	33
2002–004–2	Ms Jillian Pearsall–Jones (Curtin University Of Technology) A/Prof Jan Piek; Dr Lyndall Steed; A/Prof Florence Levy; Prof F Xavier Castellanos Monozygotic Twins Discordant for Developmental Coordination Disorder and Attention Deficit Hyperactivity Disorder: An Integrated Approach to the Bio-Psycho-Social Correlates	2002– ACTIVE – DATA ANALYSIS	42
2002–004–3	Prof David Hay (Curtin University Of Technology) A/Professor Florence Levy, A/Professor Jan Piek Solving the Jigsaw! Understanding biological and environmental effects on ADHD through discordant monozygotic twins.	2004–2009 ACTIVE – PROTOCOL CHANGE	30
2002–004–4	Prof David Hay (Curtin University Of Technology) Main Principal Investigator: Abdullah R Sheikhi (PhD Candidate) Co-Investigators: A/Professor Florence Levy, A/Professor Jan Piek Two Approaches to the Molecular Genetic Analysis of ADHD Subtypes in Australian Twins	2004–2009 ACTIVE – DATA ANALYSIS	31
2002–004–5	Prof David Hay (Curtin University Of Technology) Main Principal Investigator: Megan McDougall (PhD Candidate) Co-Investigators: A/Professor Florence Levy, A/Professor Jan Piek Family and Sibling Relationships When Twins Are Discordant for Attention Deficit Hyperactivity Disorder (ADHD)	2004–2008 ACTIVE – DATA ANALYSIS	32
2002–004–6	Prof David Hay (Curtin University Of Technology) Main Principal Investigator: James Dent (PhD Candidate) Co-Investigators: A/Professor Florence Levy, A/Professor Jan Piek Developmental correlates of reactive and proactive regression (RA/PA) (TBC)	2004–2007 ACTIVE – RECRUITING	33
2002–004–7	Prof David Hay (Curtin University Of Technology) A/Professor Florence Levy Genetic Comparison of two measures of Attention Deficit Hyperactivity Disorder (ADHD). Twin and Sibling Questionnaire: Supplement (A Study on the Behaviour of Children in Families with Twins)	2005– APPROVED	–



APPENDIX 1

Full List of Approved ATR Studies

Study No.	Researchers and Study Title	Time Frame	Page
2002-005	Dr Rodney Sinclair (St Vincent's Hospital) Common Baldness, Dandruff and Greying of Hair in Twins	2002-2003 COMPLETED	43
2003-001	A/Prof Robyn Guymer (The University Of Melbourne) Dr Paul Baird, Dr Matthew Chamberlain Genetic & Environmental Risk Factors in Age-related Macular Degeneration – A Twin Study	2003-2008 ACTIVE – ONGOING PROGRAM	29
2003-001-1	Dr Paul Baird (The University Of Melbourne) Dr Robyn Guymer, Mohamed Dirani Genetic & Environmental Risk Factors in Myopia – A Twin Study (GEM)	2004-2007 ACTIVE – DATA ANALYSIS	26
2003-002	Prof Nick Martin (Queensland Institute Of Medical Research) The Genetics of Borderline Personality Disorder (Personality Features in Adulthood)	2003-2006 ABANDONED	38
2003-003-1	Prof Nick Martin (Queensland Institute Of Medical Research) Molecular Epidemiology of Alcoholism 1: Candidate Gene (IRPG 1)	2003-2006 ACTIVE – DATA ANALYSIS	39
2003-003-2	Prof Nick Martin (Queensland Institute Of Medical Research) Variations in the effects of alcohol on liver function (IRPG5)	2003-2008 ACTIVE – DATA ANALYSIS	40
2003-003-3	Prof Nick Martin (Queensland Institute Of Medical Research) Molecular Epidemiology of Alcoholism 3: EDAC Families (IRPG3)	2003-2006 ACTIVE – DATA ANALYSIS	40
2004-001	Prof Grant Townsend (The University Of Adelaide) A/Prof Kim Seow (UQ), A/Prof Theo Gotjamanos (UWA), Dr Toby Hughes (UA), Prof Lindsay Richards (UA). Tooth Emergence and Oral Health in Twins and Their Families	2004-2009 ACTIVE – ONGOING PROGRAM	45
2004-002	Prof David Hay (Curtin University Of Technology) Associate Prof Florence Levy, School of Psychiatry, University of NSW Associate Prof Jan Piek, School of Psychology, Curtin University of Technology Investigations of ADHD: Magnetic Resonance Imaging	2004-2005 ACTIVE – DATA ANALYSIS	32
2004-003	Prof John Wark (The University Of Melbourne) A/Prof Terence O'Brien, Ms Lynda Paton, Prof Sam Berkovic, Prof Phillip Sambrook, A/Prof K Bennell, Dr Sandra Petty The Effect of Anti-Epileptic Medications on Bone Mineral Density, Balance and Fracture Risk – A Twin and Sibling Study (AED Twin Study)	2004-2009 ACTIVE – RECRUITING	49
2004-004	Prof John Wark (The University Of Melbourne) Ms Catherine Segan, Dr Richard Osborne, Assoc Prof Caryl Nowson, Assoc Prof Peter Ebeling (CIs), Prof Phillip Sambrook, Prof John Hopper, Dr Ronald Borland, Prof Nick Martin (Als) 1. Cross-sectional, within-pair comparison of smoking discordant twins. 2. Smoking cessation and indices of bone health: a co-twin trial (Twin Smoking Study 1 (Discordant) and Twin Smoking Study 2	2004-2007 ACTIVE – RECRUITING	50
2004-007	A/Prof Tracey Wade (Flinders University Of South Australia) Risk factors for the development of eating disorder phenotypes and endophenotypes in adolescent twins (Risk factors for the development of eating disorders in adolescent twins)	2004-2007 ACTIVE – ONGOING PROGRAM	47

Study No.	Researchers and Study Title	Time Frame	Page
2005-002	Prof David Hay (Curtin University Of Technology) Prof Nick Martin Prof Richard Todd Prof Florence Levy Molecular Genetics of Inattention in Australia	2005-2010 ACTIVE – RECRUITING	34
2005-003	Dr Julian Trollor (Prince Of Wales Hospital) The Twin Study of Brain Ageing and Cognition (The Twin Study of Brain Ageing and Cognition)	2005-2011 ACTIVE – RECRUITING	47
2006-001	Dr Michael Lynskey (Washington University) Prof Nick Martin Cannabis and Other Illicit Drug Use: A Twin Study	2006-2010 ACTIVE – RECRUITING	35
2006-002	Prof John Hopper (MEGA Epidemiology) SBS Insight Twins Program	2006- COMPLETED	—
2006-003	Dr Paul Baird (The University Of Melbourne) Mr Robert van de Berg Myopia Sub-Study: Myopia and Personality (Myopia and Personality)	2006-2007 COMPLETED	26
2006-004	Prof Suzanne Garland (Royal Women's Hospital) A/Pr Dorota Gertig, Prof John Wark, A/Pr Sepehr Tabrizi, Prof Marian Pitts, Dr Bircan Erbas Genetic and environmental factors in invasive cervical cancer: a twin study (Cervical Cancer)	2006-2009 ACTIVE – RECRUITING	28
2006-005	Prof Karen Thorpe (Queensland University of Technology) Compromised or competent? A longitudinal study of twin children's social competencies, friendships and behavioural adjustment. (Primary School Transition)	2009-2008 ACTIVE – RECRUITING	45
2006-006	Prof Tien Wong (University Of Melbourne) Dr Cong Sun (PhD student) Genetic and environmental contributions to retinal microvascular signs in Australian twins. (Retinal)	2006- ACTIVE – DATA ANALYSIS	37
2007-001	Dr David Greene (Australian Catholic University) Associate Professor Geraldine Naughton, Director – Centre of Phys Activity Across the Lifespan (CoPAAL) Australian Catholic University Cortical and trabecular bone mass response to 12 month calcium and vitamin D supplementation in monozygotic preadolescent females (Calcium and Bones in Pre-Teen Girls)	2006-2007 ACTIVE – RECRUITING	28
2007-002	A/Prof Jane Halliday (Murdoch Childrens Research Institute) Impact of Folic Acid (FA) on Perinatal Outcome of Twins (Perinatal Folate)	2006-2008 ACTIVE – RECRUITING	29
2007-003	Dr Anthony (Tony) Marks (University of New England) Dr Donald Hine, University of New England Professor Brian Byrne, University of New England The heritability of rational (analytical) versus experiential (intuitive) reasoning: A pilot study (Heritability of Reasoning: Pilot)	2006- ETHICS	36
2007-004	A/Prof Diane Fatkin (Victor Chang Cardiac Research Institute) A/Prof Jaime Vandenberg, Electrophysiology and Bioinformatics Program, VCCRI Statistical collaborator – TBC Dr Katrina Scurrah Role of genetic and environmental factors in atrial fibrillation (Atrial Fibrillation)	2006-2009 APPLICIATION	27



APPENDIX 2

Publications List

BOOK SECTION

Bennett, K. S., F. Levy, et al. (2007). Behaviour Genetic Approaches to the study of ADHD. *Handbook of attention deficit hyperactivity disorder*. M. Fitzgerald, M. Bellgrove and M. Gill. West Sussex, England, John Wiley and Sons: 111–128.

Byrne, B., R. K. Olson, et al. (*in preparation*). Tasking the learning in learning to read seriously: Evidence from intervention and twin studies (tentative title). *Scientific Studies of Reading*.

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Levy, F., K. S. Bennett, et al. (2006). A twin study of conduct disorder and ADHD: Is extreme Conduct Disorder different? *Attention-deficit/ hyperactivity disorder (AD/HD) and the hyperkinetic syndrome (HKS): Current ideas and ways forward*. R. Oades. New York, Nova Science Publishers: 23–34.

Noller, P., C. Conway, et al. (*In press*). Sibling relationships in adolescent and young adult twin and non-twin siblings: Managing competition and comparison. *Social relationships: Cognitive, affective and motivational processes*. J. Forgas and J. Fitness. New York, Psychology Press.

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Bigault, O., S. N. Shekar, et al. (*In prep*). "High heritability of refractive error and axial length. The Twins Eye Study."

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Corruccini, R. S., G. Townsend, et al. (2005). "Correspondence between enamel hypoplasia and odontometric bilateral asymmetry in Australian twins." *American Journal of Anthropology* **126**: 177–182.

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Gosden, R. G., S. A. Treloar, et al. (2007). "Prevalence of premature ovarian failure in monozygotic and dizygotic twins." *Hum Reprod* **22**(2): 610–5.

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CONFERENCE PROCEEDINGS

Bennett, K. S., D. Hay, et al. (2005). *Refining the phenotype of ADHD: The molecular genetics of inattention in Australia*. Sixth Annual Meeting of the ADHD Molecular Genetics Network, Miami, USA.

Bockmann, M., N. Gully, et al. (2006). *Colonisation and transmission of Mutans streptococci in Australian twins and their families*. Colgate Australia Clinical Dental Research Centre Research Day, Adelaide, Australia.

Byrne, B. (2005). *Genes and environment in early literacy and language*. University of London, Institute of Education, London.

Byrne, B. (2005). *Longitudinal twin study of early literacy and language*. Annual Conference of the International Dyslexia Association, Denver.

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APPENDIX 2

Publications List

- Byrne, B.** (2005). *Longitudinal twin study of early literacy and language: The first three years*. 12th Annual Conference of the Society for the Scientific Study of Reading, Toronto.
- Byrne, B.** (2006). *Genetic and environmental influences on early literacy: Current science and its implications*. 14th Annual International Conference of the Lindamood-Bell Workshops, Los Angeles.
- Byrne, B. and et al.** (2006). *Learning-based and 'static' measures in early literacy: A behavior-genetic analysis*. 13 Annual Conference of the Society for the Scientific Study of Reading, Vancouver.
- Chamberlain, M., P. Baird, et al.** (2005). *Heritability and novel risk factors of early age-related macular degeneration (AMD)*. Royal Australian and New Zealand College of Ophthalmologist Annual Conference, Hobart.
- Chamberlain, M., P. Baird, et al.** (2005). *Heritability of clinical features of Age-related macular degeneration – A twin study*. American Research in Vision and Ophthalmology.
- Dirani, M.** (2005). *The heritability of refraction errors and ocular biometrics*. CERA Department Meeting, Melbourne.
- Dirani, M.** (2005). *The heritability of refraction errors and ocular biometrics – A twin study*. Vision CRC Postgraduate Review Week.
- Dirani, M. and P. Baird** (2005). *The genetic component to myopia – A classical twin study*. Ophthalmic Alumni Scientific Meeting.
- Dirani, M. and P. Baird** (2005). *The heritability of myopia – A twin study*. OAA Victorian Branch Scientific Meeting, Melbourne.
- Dirani, M. and P. Baird** (2005). *Myopia in Twins*. Ocular Genetics unit meeting, Melbourne.
- Dirani, M., M. Chamberlain, et al.** (2005). *Concordant Bilateral Duane's Retraction Syndrome (type 1) in Female Monozygotic Twins*. 37th Annual Scientific Congress of the Royal Australian and New Zealand College of Ophthalmologists.
- Dirani, M., M. Chamberlain, et al.** (2005). *Identifying the genetic component to myopia – a twin study*. GeneMapper's 2005: 5th Australasian Human Gene Mapping Conference, Mt Buller, Victoria.
- Dirani, M., M. Chamberlain, et al.** (2005). *Identifying the genetic component to myopia – A twin study*. Australian Ophthalmology and Vision Sciences Meeting.
- Hay, D.** (2006). *Keynote Speaker. Genes, environment, gene-environment interaction: Where will the genetics of child psychopathology be in 2010?* 17th World Congress of the International Association for Child and Adolescent Psychiatry and Allied Professions, Melbourne, Australia.
- Hay, D.** (2006). *The role of twin studies in ADHD*. NIMH: Molecular Genetics Conference, Brussels, Belgium.
- Hay, D., N. Martin, et al.** (2007). *Is there a genetic basis to DARC (Deficits of Attention, Reading and Co-ordination)?* International Society for Child and Adolescent Psychopathology, London, England.
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- Hughes, T., G. Townsend, et al.** (2006). *The genetic basis of primary tooth emergence*. Colgate Australia Clinical Dental Research Centre Research Day, Adelaide, Australia.
- Levy, F., K. S. Bennett, et al.** (2005). *A twin study of conduct disorder and ADHD: Is extreme conduct disorder different?* International Society of Research in Child and Adolescent Psychopathology, New York, USA.
- Martin, N., K. S. Bennett, et al.** (2005). *Attention Deficit Hyperactivity Disorder and Reading Disability: Results of latent class analyses*. Sixth Annual Meeting of the ADHD Molecular Genetics Network, Miami, USA.
- Martin, N., D. Hay, et al.** (2007). *DARC: Deficits of attention, reading and coordination*. Australasian Human Development Association (AHDA) Conference, Sydney, Australia.
- Martin, N., J. Piek, et al.** (2007). *DCD and ADHD: A genetic study of their shared etiology*. 8th Motor Control and Human Skill Conference, Fremantle, Australia.
- Martin, N. C., D. Hay, et al.** (2006). *DARC: Deficits of attention, reading and coordination*. 17th Eunethydis Meeting, Bruges, Belgium.
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- McDougall, M., D. Hay, et al.** (2006). *Family and sibling relationships when twins are discordant for attention deficit hyperactivity disorder*. 17th Eunethydis Meeting, Bruges, Belgium.
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- Pearsall-Jones, J., J. Piek, et al.** (2007). *Monozygotic twins discordant for attention deficit hyperactivity disorder and developmental coordination disorder: Genetics, epigenetics and environmental effects*. Australasian Human Development Association (AHDA) Conference, Sydney, Australia.
- Piek, J.** (2007). *The relationship between motor difficulties and developmental disorders*. Australasian Human Development Association (AHDA) Conference, Sydney, Australia.
- Rigoli, D., J. Piek, et al.** (2007). *Depression and anxiety in children with attention deficit hyperactivity disorder and/or developmental coordination disorder*. Australasian Human Development Association (AHDA) Conference, Sydney, Australia.
- Townsend, G., T. Hughes, et al.** (2006). *The dentitions of monozygotic twin pairs: focussing on the differences rather than the similarities*. Current Trends in Dental Morphology, Lodz Poland, University of Lodz Press.
- Townsend, G., L. Richards, et al.** (2007). *Explaining the causes of phenotypic variation in the teeth of twins*. 12th International Congress on Twin Studies, Ghent, Belgium.
- Townsend, G., K. Seow, et al.** (2006). *The genetic basis of primary tooth emergence*. 84th General Session, International Association for Dental Research, Brisbane, Australia.
- Treloar, S. A.** (2007). *Research update on endometriosis*. Endometriosis Association (QLD) Inc. Information seminar, Brisbane Private Hospital.
- Wade, T.** (2005). *Epidemiology and long-term course of eating disorders in an Australian twin cohort*. Australian and New Zealand Academy of Eating Disorders, Sydney, Australia.
- Wade, T.** (2005). *Use of latent trait analysis to identify eating disorder phenotypes in an adult Australian twin cohort*. Eating Disorder Research Society, Toronto, Canada.
- Wade, T.** (2006). *Shared personality risk factors for anorexia nervosa: A twin study*. Eating Disorder Research Society, Port Douglas, Australia.