

The Western Australian Pregnancy Cohort (Raine) Study

2015 Activity Report

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SUMMARY

The Raine Study is one of the largest successful prospective cohorts of pregnancy, childhood, adolescence and now young adulthood to be carried out anywhere in the world. Since its inception in 1989, more than \$29 million has been invested in the Raine Study. Over 70% of the original cohort remain active participants. They are around 27 years of age and maintain a keen sense of commitment to the Raine Study.

The Raine Study is a rich resource for researchers. Prospective longitudinal data has been collected at multiple time-points through pregnancy, infancy, childhood, adolescence and young adulthood. There is broad multidisciplinary data on physical, mental and social aspects of development. The cohort has been genotyped. Data linkage with other publically held datasets, *e.g.* school results and hospital records is available. The current phenotypic dataset contains more than 70,000 measurements, 20 million genetic variants on each cohort participant over 170,000 stored biological samples. There are established collaborative research networks across a wide variety of disciplines with 19 new national or international collaborative projects starting in 2015 (*Appendix 4*).

The Raine Study has contributed to over two decades of scientific discovery with over 400 publications in peer reviewed scientific journals.

In 2015 core funding was received from The University of Western Australia (UWA), Curtin University, The Telethon Kids Institute, Raine Medical Research Foundation, UWA Faculty of Medicine, Dentistry and Health Sciences, Women and Infants Research Foundation and Edith Cowan University. Additional funds were obtained from access fees included in project grants. This funding covers the cost of the core activities of the Raine Study. Competitive grant funding covers cohort follow up and research project costs (*Table 1*).

Eighteen Raine Study competitive grant applications were submitted in 2014 to undertake research activity in 2015. Six of these grants totalling \$2,957,542 were successful. Eleven project grant applications totalling \$8.4 million were submitted in 2015 for funding for research projects to commence in 2016 (*Figures 1 & 2 and Appendix 1*).

The number and quality of peer reviewed published Raine Study papers has increased over the past 20 years with 53 publications in 2015 and a further five in press. 26% of publications appeared in journals with an impact factor greater than 5 (*Figure 3 and Appendix 5*).

In 2015 there were 35 students working with the Raine Study, 19 of whom were enrolled for Doctor of Philosophy (PhD) (*Figure 4 and Appendix 3*). Two Raine Study PhD top-up scholarships were awarded (Dr Sunil Bhat and Dr Anahita Hamidi).

For the first time since the cohort was 17 years of age, information was collected on the Raine Study parents. Preparation for the assessment of the offspring of the Raine Study participants was also initiated. Concurrent intergenerational studies required a naming system to differentiate between the projects. Parents were named *Generation 1* (Gen1), the participants *Generation 2* (Gen2) and their offspring *Generation 3* (Gen 3).

The assessment of the Raine Study parents started in January 2015, funded by NHMRC 1084947, P Eastwood et al, *Prevalence, phenotype and genotype of common sleep disorders*.

The objective of this study is to establish the basis of sleep disorders. In 2015 over 300 parents underwent physical assessment, provided biological samples and had a full sleep study at the UWA Centre for Sleep Science. Data collection will continue throughout 2016.

A project funded by ARC grant, S Parker et al, *Work design matters: the dynamic interplay of work and person factors*, commenced in 2015. The study is examining how personality and demographics shape or constrain an individuals' work. A comprehensive online questionnaire was developed and data collection processes started.

The team funded by NHMRC 1080492, Pat Holt et al, *Waxing and waning of asthma during transition from teens to adulthood*, completed the analysis of previously collected Raine Study sputum samples in relation to the trajectory of asthma associated airway disease between the ages of 14 and 22. Work is continuing on this project.

The Raine Study is involved in piloting a novel way of measuring breast density using Transillumination Breast Spectroscopy (TiBS) which measures differences in breast composition using visible and near infra-red light. This system was piloted on UWA student volunteers and will be included in measures in the Raine Study cohort assessment in 2016.

A project funded by NHMRC 1059711, RC Huang et al, *The cycle of obesity two generations of a pregnancy cohort to investigate obesity epigenetics*, is well underway with Epigenome-Wide Association Studies (EWAS) measurements obtained from a MH450K array currently under analysis, with numerous projects using these data in progress.

The WA Data Linkage System (WADLS) successfully managed the linkage of Raine Study data with WADLS managed administrative records. This linkage enabled researchers to examine the associations between Raine Study diet data with educational outcomes data collected by the WA Department of Education.

In January 2015 the Raine Study moved offices to UWA and was incorporated into the School of Population Health. The new location provides an increase in administrative office space, meeting rooms and assessment rooms.

In 2015 the Raine Study Executive Committee welcomed Professor Robyn Owens as the Committee Chairperson.

In 2015 a new Raine Study Genetics Advisory Subcommittee was formed to advise the Executive Committee on research issues related to Raine Study genetic resources. A new Raine Study Biological Samples Advisory Subcommittee was formed to advise the Executive Committee on access and research issues related to Raine Study biological samples.

In 2015 the Raine Study Secretariat processed 144 new applications for access to Raine Study resources and reviewed 41 new manuscripts (*Figure 5*).

Major challenges for the Raine Study are cohort attrition, securing future funding, keeping abreast with scientific advances e.g. whole genome sequencing and developing integrated administrative systems to align with the success and continued growth of the Raine Study.

The Raine Study Executive Committee and representatives from key partner organisations met to discuss the future of the Raine Study and agreed to support a process to identify and address current and future project needs. A successful application to Lotterywest provided funding for the appointment of consultants to perform a comprehensive review of the current

purpose, governance, funding, cohort engagement and knowledge translation activities, and provide strategic, evidence based recommendations to secure the future of the Raine Study. The final report was presented to the Executive Committee in November 2015. Discussions with core funding partners will occur throughout 2016 in order to implement many of these recommendations.

The Raine Study has an established Representative Group who have met regularly since they were 10 years old. In 2015 the Representative Group, along with other Raine Study participants met with the consultants to discuss the future direction of the Raine Study and the role and requirements of the Raine Study participants.

The inaugural *Science on the Swan* meeting was held in April 2015. The Raine Study was well represented and it was highlighted how Raine Study research is a truly collaborative project spanning most universities and research Institutes across WA.

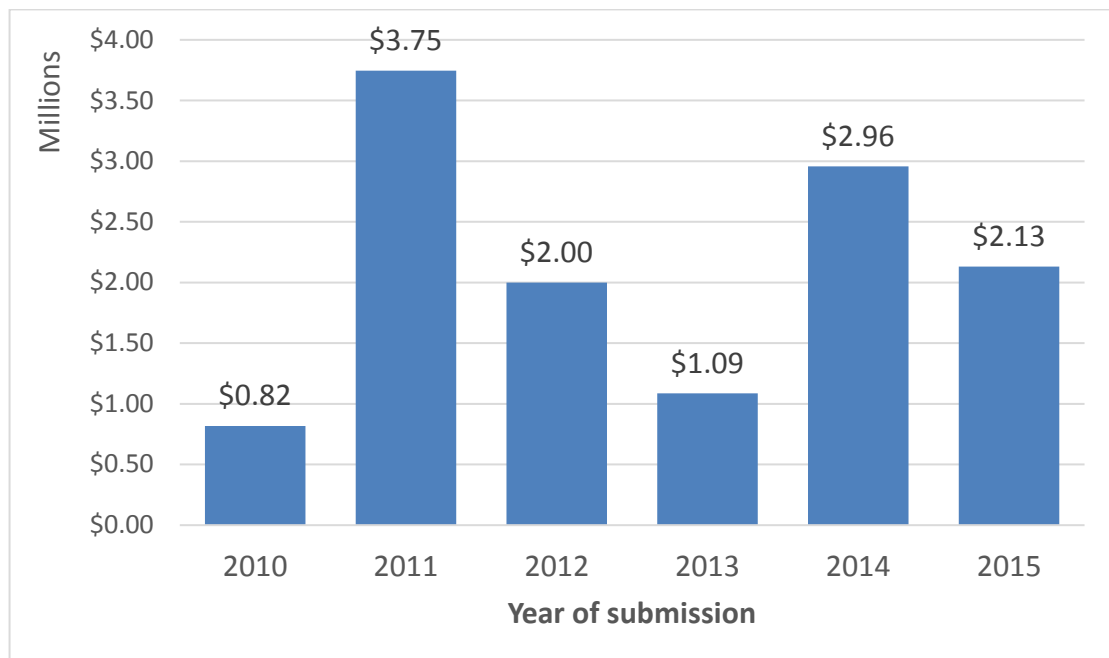
The eighth Raine Study Annual Scientific meeting was held on Friday 18 September 2015 at the University Club, UWA. The meeting was opened by the Governor of Western Australia, Raine Study Patron (and Raine Study parent), Her Excellency the Honourable Kerry Sanderson AO. The Raine Study also featured in media articles and the world press during 2015.

The Raine Study has been recognised by the Western Australian Health Translation Network (WAHTN) as a unique resource strengthening and enabling areas of excellence in health research and translation in WA.

Figure 1: Raine Study grant applications: total number submitted and total number of successful applications¹



Figure 2: Raine Study grant success: total amount awarded by year¹ (\$ millions)



¹ Year of grant submission. Payment is awarded in the year following submission. For details of successful grant applications see Appendix 1.

Figure 3: Number of Raine Study publications by year and impact factors*

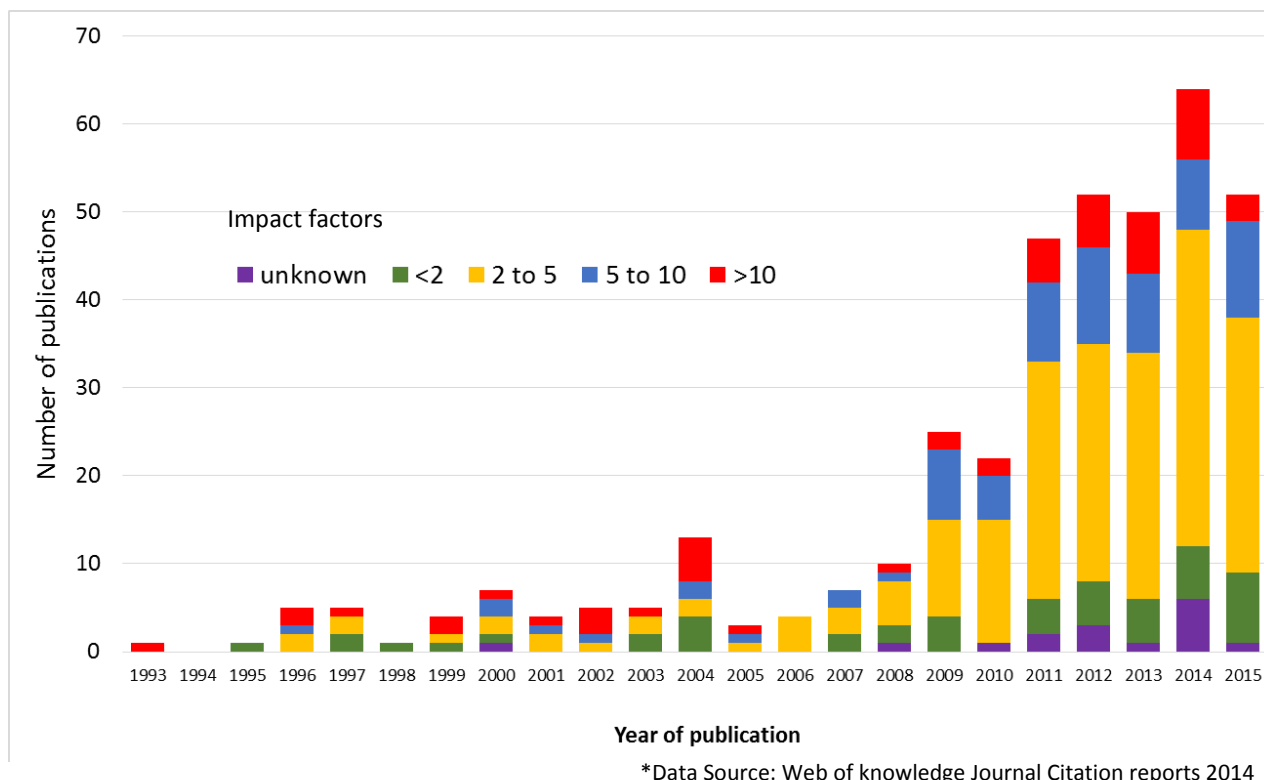
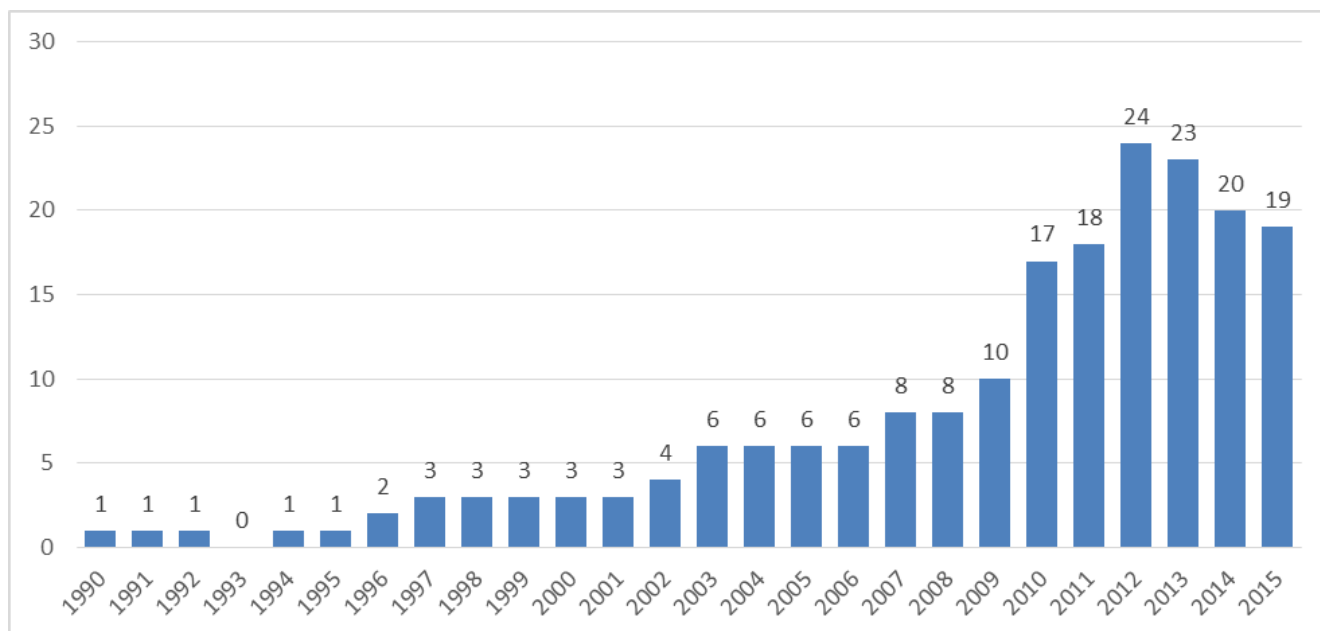


Figure 4: Raine Study PhD students: number enrolled each year



RAINE STUDY - OVERVIEW

- From 1989 to 1990 Professor John Newnham, Professor Con Michael, Professor Lou Landau and Professor Fiona Stanley recruited over 3,000 pregnant women into a study to examine ultrasound imaging, and establish a cohort of the children born to these women to determine how events during pregnancy and childhood influence health in later life. This cohort of 2868 children, the Raine Study cohort, has been followed closely over the last 26 years by a collaborative team of researchers from The University of Western Australia (Schools of Women & Infants Health, Medicine & Pharmacology Population Health, Psychology and Anatomy & Physiology), the Telethon Kids Institute, the Harry Perkins Institute of Medical Research, Curtin University, Edith Cowan University, the University of Notre Dame and the Lions Eye Institute.
- The Raine Study cohort is one of the largest, successful prospective cohorts of pregnancy, childhood and adolescence and now adulthood to be carried out anywhere in the world. The participants, now with an average age of 26, have been routinely assessed twelve times since their mothers were recruited at 16 to 18 weeks of pregnancy.
- The Study has stored biological samples collected during pregnancy, at birth, at 5, 14, 17, 20 and 22 years of age.
- The current phenotype dataset contains more than 70,000 measurements and 20 million genetic variants on each cohort participant.
- The Raine Study cohort is well established and there is frequent contact between enrolled families and study organizers. The Study has high retention rates, with over 2000 (70%) of the original cohort participants (n=2868) still involved in study activities. There is enthusiasm amongst participants to provide high quality information.
- The Raine Study families are broadly representative of the WA population; hence, research findings from this study can be translated to Western Australians.
- The Raine Study is a valuable resource for WA researchers. There are currently more than 200 researchers utilising the Raine Study. The investigators bring expertise from 25 broad areas of research including asthma and atopy; cardiovascular and metabolic health; childhood development; dental health; diabetes; epigenetics; genetic epidemiology; gastroenterology; growth; infection and immunity; mental health; musculoskeletal development; nutrition; physical activity; ophthalmology; pregnancy and birth; reproductive health; sleep; and risk taking behavior.
- There is considerable collaborative research undertaken between Raine Study investigators. Moreover, national and international research collaborations with the Raine Study are extensive and continuing to develop – these add great value to the cohort's data and expands research and funding opportunities (*Appendix 4, new collaborations 2015*). The Raine Study is a member of 14 consortia established to amalgamate genome wide association data.
- There has been an exponential increase in publication output numbers over the last five years, whilst maintaining a high average quality of journals (*Figure 3, Appendix 5*).

- The Raine Study is an invaluable resource for future young investigators and graduate students. As the cohort ages the value of the Raine Study will increase substantially. The Raine Study has all of the assets required to generate high quality research for the next five decades.
- The future continuation and success of the Raine Study is important as it known that both genes and the environment of mother, baby, child and adolescent are key contributors to diseases and conditions that account for approximately one third of the global burden of disease, in both developed and developing countries. This prospectively collected extensive data resource can assist in unraveling the complex interaction of multiple factors in the pathways to health and disease over the life course.

FUNDING UPDATE

Background

Prior to 2009 funding for the management, infrastructure and cohort assessment was obtained from research grant applications with the majority of funding provided by NHMRC program grants awarded to Fiona Stanley and colleagues at the Telethon Kids Institute (formerly the Telethon Institute for Child Health Research). This funding model was deemed unsustainable and in 2009 with the appointment of the inaugural Raine Study Scientific Director, one of the primary objectives was to obtain secure funding for Raine Study core management and infrastructure, independent of research grants.

In 2009/2010 a five year funding commitment to Raine Study core management costs was obtained from the University of Western Australia, Faculty of Medicine, Dentistry and Health Sciences, the Women and Infants Research Foundation, the Telethon Kids Institute and the Raine Medical Research Foundation. A five year matched-funding commitment was obtained from the UWA DVC (Research) and a three year commitment from Curtin University. Additional core funding was obtained from the introduction of a 15% Raine Study access fee applied to all research grant applications.

In 2014 at the end of the five year period (2009-2013), the funding commitment from these Institutions was generously renewed for a further five years, increased in line with university salary costs. A three year funding commitment was also generously provided by Edith Cowan University.

The cost of core management of the Raine Study is approximately \$600K per annum. This cost includes management of the study and maintaining contact with the cohort and facilitating current and future projects. Core funding does not contribute to costs associated with cohort assessment and data collection which requires an additional \$500-\$700K per annum depending on the specific nature of the cohort assessment research protocols.

CORE FUNDING

Core management funding covers the costs associated with:

- Remuneration of the Raine Study Secretariat (Scientific Directors, Study Manager, Study Data Managers, administrative support)
- Cohort retention and consumer consultation
- Raine Study PhD top up scholarships
- The Raine Study Annual Scientific Meeting
- The Raine Study website development and maintenance
- Management, curation and storage of previously collected data including biological samples and the purchase of storage freezers
- Cohort assessment expenses not funded by research grant funding

GRANT APPLICATIONS 2014 (for 2015)

Eighteen project grant applications were prepared and submitted in 2014 for research projects to commence in 2015. Six applications were successful.

- Successful NHMRC applications:
 - NHMRC 1084947, 2015-2017, P Eastwood, D Hillman, E Moses, N McArdle, P Melton, Prevalence, phenotype and genotype of common sleep disorders, \$1,419,000.
 - NHMRC 1080492, 2015-2017, P Holt, E Hollams, A Bosco, D Strickland, Waxing and waning of asthma during transition from the teens to adulthood, \$649,492.
- Successful ARC grant application:
 - ARC 150103312, 2015-2017, S Parker, P Dunlop, L Straker, K Parkes, Work design matters: The dynamic interplay of work and person factors, \$334,119.
- Successful applications to WA Department of Health:
 - WADH Future Health, G06302, 2014-2015, P Eastwood, L Straker, J Mountain, Western Australian Pregnancy Cohort Study, \$200,000.
 - WADH Targeted Research fund, July 2014-June 2016, S Foster, G Trapp, L Wood, W Oddy, K Allen, M Knuiman, S Zubrick, Alcohol outlet proximity and density: Implications for alcohol consumption patterns and mental health in adolescents and young adults, \$156,000.
- Successful National Breast Cancer Foundation Grant:

NBCF, PS15-040, 2015-2016, J Stone, M Hickey, L Lilge, C Saunders, J Hopper, L Carlson, A novel method to measure breast density in young women, \$198,931.

GRANT APPLICATIONS 2015 (for 2016)

Eleven project grant applications totalling \$8.4 million were prepared and submitted in 2015 for research projects to commence in 2016. Seven grants proposed the collection of data in a new cohort assessment, and four grants were to utilise previously collected Raine Study data (*Appendix 1*).

Two grant applications were successful:

NHMRC 1102106, 2016-2020, T Mori, L Beilin, E Moses, G Watts, L Adams, Genetic and early life predictors of ectopic fat and their association with cardiometabolic health and disease, \$1,706,136.

NHMRC 1109057, 2016-2018, P Eastwood, A Mian, N McArdle, D Hillman, Predicting obstructive sleep apnoea using 3D craniofacial photography, \$424,715.

GRANT FUNDED ACTIVITY 2015

NHMRC 1084947, 2015-2017, P Eastwood, D Hillman, E Moses, N McArdle, P Melton, Prevalence, phenotype and genotype of common sleep disorders, \$1,419,000.

This project commenced in January 2015 and occupied the majority of Raine Study Team activity during 2015. The grant application funded the physical assessment and overnight sleep study of the parents of the Raine Study participants. Disturbed sleep is common in the Australian community and the objectives of the study are to establish the prevalence, phenotype and genetic basis of sleep disorders, particularly obstructive sleep apnea, insomnia, restless legs syndrome and periodic leg movement syndrome in middle aged people. Together the parent and children datasets will determine associations between parent and child sleep disorders and lead to the discovery of genetic variants associated with common sleep disorders.

Project approval from UWA Human Research Ethics Committee (HREC) was granted in February 2015. All study protocols, materials and resources were created and obtained. New casual research staff were recruited and trained (*Appendix 2*). Online questionnaires, with the option of paper copies were created. Pilot assessments were conducted and the follow up commenced in May 2015. Parents of Raine Study participants who completed an overnight sleep study during the 22 year cohort follow up were invited to attend an overnight sleep study at the UWA Centre for Sleep Science. In addition, other tests including eyesight

measurements, a DXA scan, lung function testing, pressure and cold pain testing, computer based cognitive functioning test, blood pressure, anthropometric testing, accelerometry and the provision of a fasting blood sample were performed. This testing was conducted in assessment rooms located in the new Raine Study premises and at the UWA Centre for Sleep Science. In 2015 nearly 300 parents were assessed. Data collection will continue in 2016.

ARC 150103312, 2015-2017, S Parker, P Dunlop, L Straker, K Parkes, Work design matters: The dynamic interplay of work and person factors, \$334,119.

This project aims to examine the working environment and how this affects an individual's health, work performance and behaviour. The study looks at how personality and demographics, and their interactions, shape or constrain individuals' opportunities to undertake high quality work and vice versa. It will also examine how family, education, and workplace factors affect the individual and their workplace. In 2015 this project received UWA HREC approval and the complex online questionnaires have been developed and piloted. The Raine Study participants' contact details were updated and the questionnaires will be sent out early in 2016. All active Raine Study participants will be contacted and invited to complete an online questionnaire in relation to themselves and their workplace.

NHMRC 1080492, 2015-2017, P Holt, E Hollams, A Bosco, D Strickland, Waxing and waning of asthma during transition from the teens to adulthood, \$649,492.

This project commenced in January 2015, and aims to identify differences within aeroallergen-specific T-helper cell (Th) memory responses in house dust mite (HDM) sensitized Raine Study participants that are associated with variations in the trajectory of asthma-associated airways disease between the ages of 14 and 22yrs. This involves parallel studies on HDM-specific Th-memory responses at both ages employing cryobanked white blood cell samples, after stratification of subjects into groups in whom asthma persisted or waned between these two ages, and/or arose de novo at age 22yrs. To date investigators have completed assays on allergen-specific antibody profiles in both age groups and analyses are in progress employing these data. Investigators are currently in the process of analysing Th-memory cell function in subgroups of these subjects, focusing particularly on sensitized children with persistent versus late onset asthma, and these investigations will continue into 2016. Additionally, studies employing multi parameter flow cytometry are also in progress, targeting T-cell and Dendritic Cell populations that have immunoregulatory functions associated with control of inflammation. The first publication coming from the laboratory based section of this study, which focuses on the function(s) of cells present in sputum samples from symptomatic versus asymptomatic HDM-sensitized 22yr olds, has been submitted to an international journal for peer review.

National Breast Cancer Foundation (NBCF), PS15040, 2015, J Stone, M Hickey, L Lilge, C Saunders, J Hopper, A novel method to measure breast density in young women, \$198,931.

Breast density is a strong predictor of breast cancer risk. Evidence of this has been derived from mammography, which is not recommended for younger women. New methods of

measuring breast density are therefore needed to bridge large gaps in knowledge regarding breast density in young women. Members of the research team have developed Transillumination Breast Spectroscopy (TiBS) which measures spectral differences in breast composition using visible and near infrared light. It correlates highly with mammographic breast density in women over 40 and is safe and easy to use. This pilot study aims to test the feasibility and acceptability of the TiBS machine to measure breast density. The investigators are conducting a pilot study on volunteers (non Raine Study participants) using this machine. The UWA HREC have granted permission for the study, Raine Study staff have been trained on the use of the TiBS machine and recruitment of volunteers is underway. The testing is conducted at the Raine Study house, UWA. It is proposed that the TiBS machine will be used in the next Raine Study Cohort follow up, following a successful pilot study.

NHMRC 1059711, 2014-2016, RC Huang, K Lillycrop, G Burdge, J Craig, L Beilin, T Mori, W Oddy, K Godfrey, J Holbrook, The cycle of obesity: Two generations of a pregnancy cohort to investigate obesity epigenetics, \$1,086,102.

The project commenced in 2014 to examine obesity epigenetics in two generations of the Raine Study. Participant DNA samples have undergone MH450K array analysis. Since completion of the HM450K arrays for the 17 year old RAINE participants the data has been cleaned and analysed and hotspots showing associations with obesity related phenotypes have been identified. These hotspots are now undergoing pyrosequencing validation in DNA samples from participants at age 17 and 20 and from parent samples and results are being generated. A manuscript related to this body of work was published.² Interesting associations are being discovered in the Raine Study analyses and further publications are currently in preparation.

WADH Future Health G06302, 2014-2015, P Eastwood, L Straker, J Mountain, Western Australian Pregnancy Cohort Study, \$200,000.

This funding was secured to analyse blood samples collected during the follow up at 22 years of age. This was completed and the data incorporated in the Raine Study database. A research officer was employed to facilitate the translation of Raine Study research scientific findings and lay summaries of published scientific journal articles were produced and published on the Raine Study website. This grant also supports the management of accelerometry data.

NHMRC 1044840, 2013-2015, L Straker, G Healy, M Tremblay, R Abbot, A Smith, G Mishra, A life course approach to characterising and predicting inactivity and sedentary behaviour of young adults, \$291,474.

This grant supported the collection and analysis of accelerometer data in the 22 year cohort follow up. Over 900 Raine Study participants wore an accelerometer recording their waking and sleeping behaviour, as well as completing an activity diary and questionnaire information

² Huang RC, Garratt ES, Pan H, Wu Y, Davis EA, Barton SJ, et al. Genome-wide methylation analysis identifies differentially methylated CpG loci associated with severe obesity in childhood. *Epigenetics*. 2015;10(11):995-1005.

on active and sedentary behaviour during the 22 year cohort follow up. Data collection was completed and data assimilation and analysis was ongoing in 2015. Poor activity habits are expected to overtake smoking as the leading preventable cause of health burden in Australia. Poor activity habits increase the risk for a shorter life and many health problems such as heart disease, some cancers and diabetes. Young adulthood is an important time for individuals to develop their lifestyle habits. This study provides the first detailed description of the inactivity habits of Australians in their early 20s. The first manuscript using these data was published in 2015.³

NHMRC 1042269, 2012-2016, R Hart, C Pennell, D Doherty, M Robinson, R Norman, The long-term consequences of IVF treatment for the offspring - a prospective cohort study using the Raine cohort for comparison, \$1,552,096.

The Growing Up Healthy Study aims to determine the long-term consequences of assisted reproduction upon the development of the offspring by comparing their growth, metabolic, respiratory, psychological, immunological and reproductive development at ages 13-15, 16-18 and 20-22 with outcomes from the Raine Study cohort. Teenagers involved in the study were invited to visit the GUHS research team at Raine Study house, UWA to undertake the same age-specific assessments performed on the Raine cohort, focusing on metabolic, respiratory, psychological, immunological and reproductive health. The study is proceeding as planned, with approximately 350 teenagers currently involved. Data collection continued during 2015, and will continue in 2016.

DATA LINKAGE

Data linkage is a technique for creating links between information from different sources that relate to the same individual, family, place or event. The Raine Study Executive Committee are the data custodians of the Raine Study data, and are responsible for protecting the privacy of the cohort individuals. Approval to link the Raine Study dataset with other publically held datasets was previously obtained from the participants, from the Raine Study Executive Committee, from WA Department of Health Ethics Committee, the WA Developmental Pathways Project and the WA Data Linkage System (WADLS). The WADLS successfully managed the linkage of some Raine Study data with WADLS managed administrative records. This linkage enabled researchers to examine the associations between Raine Study diet data with educational outcomes data collected by the WA Department of Education.^{4,5}

³ Slater JA, Botsis T, Walsh J, King S, Straker LM, Eastwood PR. Assessing sleep using hip and wrist actigraphy. *Sleep and Biological Rhythms*. 2015;13(2):172-80.

⁴ Nyaradi A, Li J, Hickling S, Foster JK, Jacques A, Ambrosini GL, Oddy WH. A western dietary pattern is associated with poor academic performance in Australian adolescents. *Nutrients*. 2015;7(4):2961-82

⁵ Nyaradi A, Li J, Hickling S, Whitehouse AJ, Foster JK, Oddy WH. Diet in the early years of life influences cognitive outcomes at 10 years: a prospective cohort study. *Acta Paediatr*. 2013;102(12):1165-73

The Raine Study management identified the opportunity for the education outcomes data to be utilised in the context of other outcome factors.

In 2015 a combined application was made to the WADLS to extend the current project to include other factors that influence educational outcomes and that educational outcomes may in turn affect. The extended project addresses two linked aims:

- 1) To explore the associations between early life, childhood and adolescent health, behaviour, genetic and environment factors and school educational achievement;
- 2) To explore the associations between school educational achievement and young adult education, workforce and social outcomes.

This research initiative was deemed by the WA Data Linkage Unit to be too large to be undertaken as a single project and work is continuing with initial approval from education data custodians to access educational data.

INTERGENERATIONAL STUDIES

The Raine Study has discussed the logistics of undertaking intergenerational cohort studies and the inclusion of grandparents, parents, siblings and offspring of cohort participants. In 2015, for the first time since the cohort participants were 17 years of age, assessment of the Raine Study parents was conducted. A project to collect information from the offspring of the Raine Study participants was also initiated. This is a great achievement for the Raine Study resource. A naming system based on Raine Study Generations (Gen) was devised to differentiate between simultaneous assessments.

Gen0	Grandparents
Gen1	Mothers and fathers originally recruited into the study
Gen2	Raine Study participants
Gen2_25	ARC funded work and personality online questionnaire at 25 yrs
Gen2_27	NHMRC funded follow up at 27 yrs
Gen3	Offspring of the Raine Study participants

Raine Study Generation 1 (Gen1) parents assessment

The Raine Study is currently collecting data on parents, the original recruits into the Raine Study between 1989 and 1991. The study is funded by NHMRC grant 1084947 and parents of Raine Study participants are invited to participate in an assessment and have a sleep study (*see page 12*).

Raine Study Generation 2 at 25 yrs (Gen2_25)

This project, funded by ARC grant is examining how family, education, and workplace factors affect the individual and their workplace. All active Raine Study participants will be contacted and invited to complete an online questionnaire in relation to themselves and their workplace (see page 13). The Raine participants will be on average 25 years old at the time of questionnaire completion.

Raine Study Generation 2 at 27 yrs (Gen2_27)

In 2016, a cohort assessment at age 27 will be initiated, funded by successful grant NHMRC 1102106, T Mori et al, *Genetic and early life predictors of ectopic fat and their association with cardiometabolic health and disease*.

Raine Study Generation 3 (Gen3)

The national Autism CRC⁶ (represented by Andrew Whitehouse in WA) is collecting detailed phenotypic information and blood samples from children diagnosed with Autism Spectrum Disorder (ASD). The primary aim of the Autism CRC is to increase understanding of the biology underpinning Autism Spectrum Disorders. To achieve this aim the Autism CRC has invested in creating a large store of phenotypic and biological data from over 1,200 Australian families that include a child with an ASD diagnosis.

The Autism CRC approached the Raine Study to collect developmental information on the offspring of the Raine Study participants to form a control group for their ASD cohort. Raine Study researchers are eager to include the next generation (offspring of the Raine Study participants) in the Raine Study. The Raine Study participants have indicated that they are keen to include their offspring as part of their role as participants in the ongoing Raine Study cohort study. This project provides an opportunity to contact and assess offspring of the Raine Study participants. Data collection is planned to start in 2016.

⁶ www.autismcrc.com.au/

RAINE STUDY ACTIVITY

2015 was a busy and productive year for the Raine Study participants, management, staff and researchers. The following section provides an overview of the main Raine Study non research activities and achievements in 2015.

Move to UWA Campus and the School of Population Health

At the end of 2014, the UWA Faculty of Medicine, Dentistry and Health Sciences approved the allocation of office space and assessment rooms at 14-16 Parkway on UWA Campus to the Raine Study. This building is located adjacent to the UWA Centre for Sleep Science and has increased capacity for office space and clinical assessment for follow up studies.

For over 20 years The Raine Study played a major role in the Telethon Kids Institute and the Raine Study thanks the Institute for its support and looks forward to maintaining established connections and strong partnerships.

In January 2015 the Raine Study moved to the UWA and the Raine Study was incorporated into the UWA School of Population Health. The Raine Study thanks Professor Colleen Fisher and all the staff at SPH for facilitating the transition, and for the warm welcome extended to the Raine Study.

Raine Study Executive Committee

In 2015 the Raine Study Executive Committee welcomed Professor Robyn Owens as the Committee Chairperson.

Professor John Challis was thanked for his contribution as interim Chair of the Committee, and congratulated on his new role as Director of the Western Australian Health Translation Network (WAHTN).

During 2015 The Committee discussed over 90 project and collaboration approval applications as well as overseeing the governance, leadership and management of the Raine Study. Their efforts, dedication and commitment to the Raine Study is acknowledged.

Raine Study Genetics Advisory Subcommittee

The Raine Study has stored biological research material provided by participants and their parents. The Raine Study Executive Committee acts as custodians of all data and biological samples. Blood and saliva have been collected from the participants and their parents over the duration of the study, in accordance to procedures approved by HRECs, the National Statement and the Privacy Act. Informed consent has been obtained from these individuals to extract, store and analyse their DNA. These DNA samples have been analysed to establish datasets of genetic information. Access to the DNA samples and to the genetic datasets is through the approval processes detailed in the Raine Study 'Data and Biological Samples Access Policy'.

In 2015 a new Raine Study Genetics Advisory Subcommittee (GAS) was formed. The role of this subcommittee is to provide advice to the Raine Study Executive Committee on research issues related to the Raine Study genetic resources.

The inaugural meeting of the GAS was held on the 11 March 2015.

Raine Study Biological Samples Advisory Subcommittee

The Raine Study has collected and stored biological research material provided by participants and their parents. The Raine Study Executive Committee acts as custodians of all data and biological samples. Various samples have been collected from the participants and their parents over the duration of the study, in accordance to procedures approved by HRECs, the National Statement and the Privacy Act. Informed consent has been obtained from these individuals to store and analyse these samples.

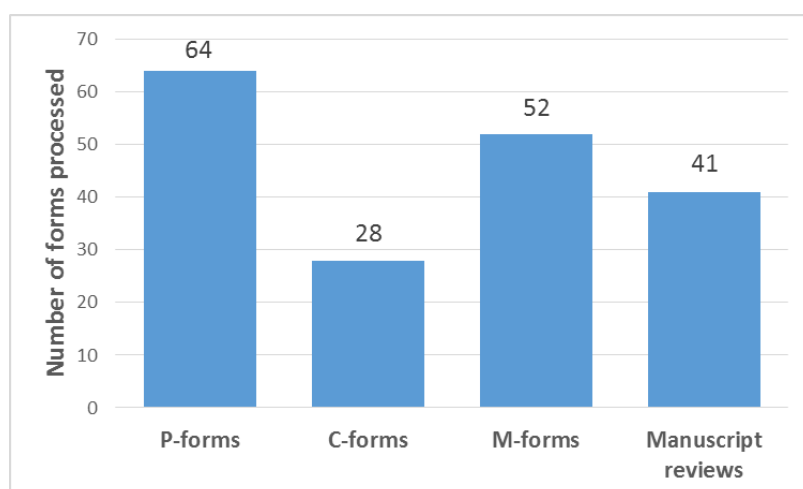
In 2015 a new Raine Study Biological Samples Advisory Subcommittee (BAS) was formed. This subcommittee provides advice to the Raine Study Executive Committee on access and research issues related to the Raine Study biological samples. The inaugural meeting of the BAS was held on 19 August 2015.

Raine Study Secretariat

The Raine Study Secretariat manage all governance and research application processes, review grant applications and manuscripts and process all data requests.

In 2015 there were 144 new applications processed and 41 new manuscripts reviewed. All new projects were associated with requests for data or cohort information.

Figure 5: Number of new applications and manuscripts reviewed in 2015



The Raine Study future scoping project

Raine Study Executive Committee members and representatives from key partner organisations (UWA, Curtin University, Edith Cowan University, Telethon Kids Institute, Women and Infants Research Foundation, the Raine Medical Research Foundation, Perkins Research Institute) met to discuss the future of the Raine Study and agreed to support a process to identify and address current and future needs of the project, specifically:

- Develop a clearer legal framework and ownership of the Raine Study assets and to explore the option of establishing a separate legal entity;
- Develop a clearer governance structure capturing the collaborative multi-institutional ownership of the Raine Study;
- Develop a business plan for ongoing funding;
- Develop an administration system to enhance quality assurance and reduce staff workloads;
- Develop a research themes and teams plan aligned to a life-course trajectory approach;
- Develop a cohort engagement/re-engagement plan;
- Develop a curation plan for biosamples, digital data and hard copy archives; and
- Develop a discovery translation plan.

In consultation with Lotterywest, a briefing document was developed and a Lotterywest grant application to fund the scoping project was successful. The Raine Study Executive Committee approved the appointment of management consultants, OBH Consulting to undertake the work in late April 2015.

OBH Consulting were tasked to ascertain the current and future needs of the Raine Study through a comprehensive review of the current purpose, governance, funding, administration, researcher engagement, cohort engagement, resource curation and knowledge translation activities. They were to explore and propose improved models to more effectively meet the stated purpose of the Raine Study, to improve operating procedures and productivity and protect the future requirements of the Study. The consultants met with stakeholders, staff and cohort participants to obtain information and an understanding of the process and functioning of the Raine Study and a Steering Committee was formed to facilitate this process.

The consultants were invited to present and discuss their interim report at the Executive Committee meeting on 28 August 2015. The Scientific Directors presented the final report at the Executive Committee meeting on 25 November 2015:

- The Committee agreed that it had been a worthwhile exercise in drawing attention to and examining areas that required attention.
- The Committee agreed in principle to the recommendations made by the Raine Study Scientific Directors in relation to the report, subject to clarification of process and cost.

- The Executive Committee agreed to explore the option of the Raine Study forming a new independent entity, *an unincorporated joint venture*, between the current major funders with manager/agent support by one or more joint venture partner.

The issues and recommendations raised will be clarified and addressed in 2016.

Raine Study Representative Group

The Raine Study fosters and encourages participant involvement in decisions about contact or communication with the cohort including assessments, cohort activities and research studies. The Raine Study has an established Representative Group who have met regularly since they were 10 years old. The Raine Study personnel and researchers meet regularly with this group and other cohort members in relation to contact with the cohort and planned research activity. In 2015 the Representative Group, along with other Raine Study participants, met with the Consultants (*see page 20*) to discuss the future direction of the Raine Study and the role and requirements of the Raine Study participants. A new Steering Committee was formed to oversee the future of this process. Membership of this committee includes five Raine Study participants.

Raine Study Students

Raine Study PhD Top up Scholarships

In January 2015 the Raine Study Executive Committee approved two PhD top-up scholarships awarded to.

- I. Dr Sunil Bhat: Supervisors Professor Lawrie Beilin, Professor Trevor Mori. Familial determinants of cardiovascular risk factors among adolescents in a longitudinal Australian birth cohort, the Raine Study.
- II. Dr Anahita Hamidi: Supervisors Professor Trevor Mori, Professor Peter Eastwood, A/Professor Rae Chi Huang. Evaluation of cardio-metabolic risk factors in adolescents and young adults: impact on cardiac function and sleep respiratory events.

In 2015 there were 35 students working with the Raine Study, 19 of whom were enrolled for Doctor of Philosophy (PhD). Four of these students obtained their doctorate degrees in 2015 (*Appendix 3*).

Science on the Swan

The inaugural *Science on the Swan* meeting was held in April 2015. The aim of this meeting was to showcase medical science and health research in WA and bring together all five of WA's major universities in partnership with the key teaching and research hospitals, the medical research institutes of WA and the WA Government through the Department of Health and the Office of Science. The Raine Study was well represented at the conference. The activities of the Raine Study served to highlight the effectiveness and productivity of a truly collaborative project spanning all the universities and research institutes across WA.

Raine Study Annual Scientific Meeting

The eighth Raine Study Annual Scientific Meeting was held on Friday 18 September 2015 at the University Club, UWA. The meeting was formally opened by the Governor of Western Australia, Raine Study Patron and Raine Study parent, Her Excellency the Honourable Kerry Sanderson AO. Highlights of the day were talks by Judy and Michael about their experience as Raine Study parents and as participants in the Raine Study parent sleep study. Two \$750 prizes kindly donated by the Raine Medical Research Foundation for best early career researcher presentations, were awarded by Professor Paul Norman to Anya Jones and Tegan Grace.

The Western Australian Health Translation Network (WAHTN)

The WAHTN is a consortium comprising all health researchers in Western Australia: Curtin University, The Department of Health, Edith Cowan University, Fiona Stanley Hospital, Fremantle Hospital, Harry Perkins Institute of Medical Research, King Edward Memorial Hospital, Lions Eye Institute, Institute of Respiratory Health, Murdoch University, Notre Dame University, Princess Margaret Hospital, Royal Perth Hospital, Sir Charles Gairdner Hospital, the Telethon Kids Institute, the University of Western Australia and the Western Australian Neuroscience Research Institute. Its vision is to achieve better health outcomes for the Western Australian community through integrated discovery, translation and clinical care delivery. Extensive cross-disciplinary and cross-institutional collaboration is core to the WAHTN's model for health care and translational research.

The Raine Study has been recognised by the Western Australian Health Translation Network (WAHTN) as a unique resource strengthening and enabling areas of excellence in health research and translation in WA.

CHALLENGES FOR THE FUTURE

Cohort attrition

Longitudinal cohort studies are sensitive to the loss of participants. It is not possible to replace those lost to the study with new participants. Therefore, it is crucial to retain participants and to try and re-engage participants who may have withdrawn or been lost to follow up. The Raine Study has been successful in retaining a high proportion of participation over the past 26 years. Cohort retention needs to be a priority area, with new strategies to maintain participation explored and implemented.

Funding for future cohort follow up assessments

The operating principle of the Raine Study has been to perform a follow-up study of the entire cohort every 3 years. Each follow-up study takes 3 years, and involves the contact and recruitment of active members of the cohort and the collection of (i) a set of questionnaire-based data and physical measurements that have been collected at previous follow-ups (termed core data, est. \$500,000 per year); and (ii) a set of measurements (questionnaire and/or physical measurements) that have been proposed by researchers to address a specific research question (usually NHMRC-funded and the cost depends on the nature of the study being proposed, but ranges from \$300,000 to \$1.5 million). If a cohort follow up is not conducted every 2 to 3 years, the risk of losing the cohort is high. The discontinuation of the Raine Study would be an enormous loss to the future of scientific discovery and our capacity for WA to be a global contributor to improving health outcomes.

To date, follow-ups have been funded by combining the funds from multiple NHMRC project grants. However such funding is becoming increasingly difficult to obtain, especially given the requirement for any project-specific grant application to include funding to support collection of core data. This requirement has meant that some applications have been deemed uncompetitive. In some instances when an NHMRC grant has been successful, the funding for core funding has been eliminated from the budget, which then places the viability of the follow-up in jeopardy. One of the current strategic goals for the Raine Study is to secure funding for regular, scheduled assessment of the cohort for recruitment and collection of core data, independent of competitive grant applications.

Whole genome sequencing

Whole genome sequencing is more sensitive and accurate than exome sequencing for the detection of genetic structural variation, and includes non-exonic regulatory regions. Previous GWAS and exome focused work produced detailed information on the 1% of the genome that codes for proteins; this new approach identifies variants in intronic and intergenic regions, where it is believed complex-disease risk variants may be found. Until now, whole genome sequencing has been prohibitively expensive and time consuming, and data analyses capabilities were ill-suited to this type of data; with the advent of 'next-generation

sequencing', it is possible to sequence the entire human genome in a day, at a cost that is accessible to the research community.

As the field of genomics advances, more cohorts and consortia will move to whole genome sequencing datasets to provide insight into the genetic and developmental origins of health and disease. Should whole genome sequencing data be generated for the Raine Cohort, this would be coupled with the broad and deep phenotype dataset, amassed from data collected from 18 weeks gestation to 22 years of age. This unique resource would enable the Raine Study to affirm its position as an internationally recognised pregnancy cohort and genomics leader, continue participating in multinational research consortia, and provide valuable insight into the origins of health and disease to researchers, clinicians and policy makers.

Integrated management and data management systems

Over the past few years the Raine Study has experienced exponential growth in relation to research activity and research output. This has impacted on the administrative workload and reporting requirements. Increased research activity has led to increased demand for data access. The Raine Study requires updated and integrated systems to manage administrative and research based processes.

RESEARCH TRANSLATION

The Raine Study has contributed to over two decades of scientific discovery. Research from the cohort has led to novel discoveries, described normal ranges for many physiological measurements, described disease prevalence, provided insights into research methodology, identified new epidemiological associations and has been used as a healthy control group in many studies.

Over the years, findings from the Raine Study have led to changes in clinical practise and social policy. For example fetal growth charts used in WA were derived from the Raine Study and have been in use for the last 20 years. Serial ultrasound scans in pregnancy have been shown to be safe and which has an impact for every pregnant woman. Normal measures for blood pressure in young children were derived from Raine Study measurements. The Raine Study demonstrated the value of breastfeeding in relation to improved respiratory health, language development, body weight and behaviour. The Raine Study established that a higher than expected proportion of teenage girls suffer from polycystic ovary syndrome (PCOS). Raine Study findings have identified sub-types of asthma in childhood, adolescence and young adulthood and has contributed to identifying ten new genetic markers for asthma and sixteen new markers affecting lung function. Exposure to life stress during pregnancy was associated with increased weight in the offspring at 20 years of age demonstrating that events during pregnancy can have long-lasting effects on the offspring. Diet quality has an effect on educational achievement and this was shown at ages 5, 12 and 14. Evidence from the Raine Study in relation to smoking during pregnancy, passive smoking and smoking in cars was used to ban smoking in cars with children and in public places.⁷

Access to the Raine Study research results is through publication in peer reviewed journals, information on the Raine Study website, media releases, engagement with Raine Study stakeholders and the dissemination of information at conferences and scientific meetings. Raine Study information is also used in evidence based population health guidelines.

Research translation takes time for evidence based research findings to change policy and behaviour.

The Raine Study has been recognised by the WAHTN as a unique resource strengthening and enabling areas of excellence in health research and translation in WA.

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[http://www.parliament.wa.gov.au/Parliament/commit.nsf/%28Evidence+Lookup+by+Com+ID%29/A1CF12960032119448257831003C10F4/\\$file/educ&health090210.4.pdf](http://www.parliament.wa.gov.au/Parliament/commit.nsf/%28Evidence+Lookup+by+Com+ID%29/A1CF12960032119448257831003C10F4/$file/educ&health090210.4.pdf)

RAINE STUDY IN THE MEDIA

Findings from the Raine Study are published by the world’s media, thereby bringing study findings to the attention of the scientific community and the general public.

In June 2015, Professor John Newnham was interviewed on ABC news in relation to the Raine Study.

*"The Raine Study was designed to find out what's the meaning of life before birth regarding your health as a child and, most importantly, as an adult."*⁸

In July 2015 The West Australian published a feature article on the Raine Study in the Health and Medicine supplement.⁹



In September 2015 Roger Hart’s male fertility study made headlines around the world.¹⁰

*Researchers call for WHO review after one-seventh meet ‘normal’ sperm count. A Western Australian study of men in their 20s, published on Friday, found only one in seven met the World Health Organisation’s male fertility criteria*¹¹

The Raine Study was cited in the WA Office of Science publication “Science Statement for Western Australia”¹². *Western Australia is also recognised for its longitudinal population health studies, ... with the Raine Study continuing to provide unique data sets that bring together some of Australia’s leading researchers and international collaborators.*

⁸ http://blogs.abc.net.au/wa/2015/06/john-newnham-who-are-you.html?site=perth&program=720_mornings

⁹ <http://health.thewest.com.au/news/2147/long-may-kids-health-study-raine>

¹⁰ Hart RJ, Doherty DA, McLachlan RI, Walls ML, Keelan JA, Dickinson JE, Skakkebaek NE, Norman RJ, Handelsman DJ. Testicular function in a birth cohort of young men. Hum Reprod. 2015;30(12):2713-24.

¹¹ <http://www.theguardian.com/australia-news/2015/sep/30/>

¹² <https://www.dpc.wa.gov.au/science/Documents/DPC.statement.web.pdf>

Appendix 1: GRANT APPLICATIONS

SUCCESSFUL GRANT APPLICATIONS - submitted in 2014 for funding in 2015

1. NHMRC 1084947, 2015-2017, P Eastwood, D Hillman, E Moses, N McCardle, P Melton, Prevalence, phenotype and genotype of common sleep disorders, \$1,419,000. **Funded**
2. NHMRC 1080492, 2015-2017, P Holt, E Hollams, A Bosco, D Strickland, Waxing and waning of asthma during transition from the teens to adulthood, \$649,492. **Funded**
3. ARC 150103312, 2015-2017, S Parker, P Dunlop, L Straker, K Parkes, Work design matters: The dynamic interplay of work and person factors, \$334,119. **Funded**
4. National Breast Cancer Foundation PS15-040, 2015-2016, J Stone, M Hickey, L Lilge, C Saunders, J Hopper, L Carlson, A novel method to measure breast density in young women, \$198,931. **Funded**
5. WA Department of Health Future Health G06302, P Eastwood, L Straker, J Mountain, Western Australian Pregnancy Cohort Study, \$200,000. **Funded**
6. Western Australian Department of Health Targeted research fund, S Foster, G Trapp, L Wood, W Oddy, K Allen, M Knuiman, S Zubrick, Alcohol outlet proximity and density: Implications for alcohol consumption patterns and mental health in adolescents, young adults, \$156,000. **Funded**

GRANT APPLICATIONS – submitted in 2015 for funding in 2016

1. NHMRC 1102106, T Mori, L Beilin, E Moses, G Watts, L Adams, Genetic and early life predictors of ectopic fat and their association with cardiometabolic health and disease, \$1,956,136. **Funded**
2. NHMRC 1109057, P Eastwood, A Mian, N McCardle, D Hillman, Predicting obstructive sleep apnoea using 3D craniofacial photography, \$424,715. **Funded**
3. NHMRC 1102223, M Hickey, J Stone, C Saunders, M Sabin, N Warrington, D Taylor, G Colditz, How does the early life environment modify breast cancer risk? A prospective cohort study, \$545,258.
4. NHMRC 1108020, A Teichtahl, A Smith, Y Wang, D Urquhart, Does the risk of hip osteoarthritis begin in childhood? Implications for prevention, \$301,451.
5. NHMRC 1102101, D Green, L Beilin, L Straker, P Eastwood, Developmental origins of adult cardiovascular disease: Vascular health in the Raine Cohort, \$1,164,955.
6. NHMRC 1101032, D Mackey, A Hewitt, C Hammond, S Macgregor, K Rose, E Milne, F Chen, M He, J Guggenheim, Young adult myopia: genetic and environmental associations, \$1,394,728.
7. NHMRC 1104349, G Ambrosini, J Scott, G Trapp, W Oddy, F Bull, Identifying opportunities to reduce non-communicable diseases: a prospective analysis of novel determinants of dietary intake and eating behaviours in the Raine Study, \$508,091.
8. NHMRC 1102574, P O'Sullivan, J Karppinen, A Borthakur, L Straker, A Smith, D Beales, K Cheung, F Williams, Understanding lumbar spine degenerative changes and their relationship to back pain and disability in young adults, \$579,306.
9. NHMRC 1099700, R Mattick, E Sillins, J Horwood, G Patton, J Najman, J Toumbourou, D Hutchinson, R Tait, R Skinner, R Hayatbakhsh, Continuity and discontinuity of cannabis use: Predictors and outcomes into contemporary adulthood, \$782,024.
10. NHMRC 1104506, W Oddy, T Mori, G Ambrosini, R Chi Huang, L Adams, Nutritional predictors of cardio-metabolic risk from infancy to adulthood, \$348,014.
11. ARC DE160101012, I Heinonen, D Green, P Eastwood, L Beilin, L Straker, Effect of maternal physical activity on adult arterial phenotype in humans, \$403,437.

Appendix 2: PEOPLE OVERVIEW

Participants: 2300 Raine Study participants, average age 26, are currently registered as “active”. Active participants have agreed to remain in the study and be contacted for future assessment.

Participant Reference group: Ten original members of Raine Study cohort (formed in 2005) with other volunteers comprise the Reference Group. This group meets regularly with Raine Study staff and researchers to discuss cohort planning and activity.

Raine Study Executive Committee: The Committee includes representation from the original investigators of the Raine Study, a representative of the Raine Medical Research Foundation and esteemed researchers with specialist knowledge and expertise. The Committee is responsible for the protection of the cohort members, upholding the scientific and ethical integrity of the research and overseeing the management of the Raine Study. Approval for research projects and access to cohort resources must be submitted in writing to the Committee. *Committee Chair:* Professor Robyn Owens, *Committee Members:* Professor John Newnham, Professor Lou Landau, Professor Lawrie Beilin, Professor Jennie Blackwell, Professor Nick de Klerk, Professor David Mackey, Professor Leon Straker, A/Professor Craig Pennell, Professor Paul Norman, Professor Susan Prescott.

Raine Study Scientific Directors: The Scientific Directors are appointed by The Executive Committee and provide leadership and strategic direction for cohort research activities. The positions are funded by the Raine Medical Research Foundation.

Raine Foundation Scientific Director, Professor Peter Eastwood, *Raine Foundation Associate Scientific Director:* Professor Leon Straker

2015 Raine Study Staff

Manager: Jenny Mountain

Data manager, biostatistician:

Angela Jacques

Co-ordinator: Diane Wood

Data manager: Louise McKenzie

Research officer: Alex D’Vaux

Phlebotomist: Sue Green

Recruitment: Chris Halliday

Data entry: Carolyn Smargiassi

Research officer: Rachel Collins

Research assistant: Monique Priston

Overnight assistants

Andrew Mountain

Zoe Marson

Alex Burton

Casual Research Assistants

Natasha Haynes

Alice O’Connor

Elisa Robey

Ruth Smith

Renee Wood

Louise Smargiassi

Sarah Findlay-Jones

Upasana Jayaraman

Maddison Jones

Michelle Tickner

Sleep Scientists

Gemma Peagno

Aaron Gazzola

Ashwin Hirupathy

Anthea Beck

Azin Mushtaq

Avijit Bose

Madeleine Lowe

Appendix 3: RAINE STUDY STUDENTS

Student	Degree	Supervisors	Title
Students who completed their studies in 2015			
Chi Le Ha	PhD, UWA 2015	L Beilin T Mori	Studies of antenatal and postnatal factors predicting cardiovascular phenotypes from birth to 17 years.
Priyakumari Ganesh Parmar	PhD, UWA 2015	L Palmer C Pennell	Network growth to understand the genetic and environmental factors underlying the Developmental Origins of Health and Disease (DOHaD).
Seyan Yazar	PhD, UWA 2015	D Mackey A Hewitt	Genetic and Environmental Factors Contributing to Variation in Corneal Structure and Disease in a Young Adult Population.
Jessica Tearne	PhD, UWA 2015	J Li M Robinson	Maternal and paternal age at birth, and developmental outcomes in offspring.
Sebastian Rauschert	Overseas student project 2015	W Oddy, B Koletzko	Analysis of Metabolic Profiles in young adults from the Raine Study
Rachel Jones	Honours UWA 2015	A Whitehouse E Moses	A genetic investigation of autistic like traits.
Michelle Trevenen	Honours, UWA 2015	P Eastwood	Development of an algorithm to measure sleep from wrist and hip accelerometry.
Current PhD Students			
Anett Nyaradi	PhD, UWA	W Oddy J Li	Examining the relationship of nutritional intake with mental health and educational outcomes among Western Australian children.
Koya Ayonrinde	PhD, UWA	J Olynyk L Adams	The epidemiology and significance of hepatic disorders in adolescents (primary focus is on non-alcoholic fatty liver disease, secondary focus hereditary haemochromatosis).
Scott White	PhD, UWA	C Pennell J Newnham S Lye	Development of an individualized programme approach to the assessment and modification of antenatal and postnatal growth.
Richard Maganga	PhD, UWA	C Pennell S Lye	Assessment of telomere length in adolescents in the Raine Study: associations between obesity, insulin resistance and fatty liver disease.
Janice Wong	PhD, UWA	M O'Donnell J Fletcher	The relationship between educational and mental health outcomes for Western Australian Children: A longitudinal population study.
Carly Herbison	PhD, UWA	C Pennell H Atkinson	The stress response in adolescents, mental health outcomes and lifestyle choices.
Denise Demmer	PhD, UWA	T Mori L Beilin	The association between fitness trajectories and adolescent clustered metabolic risk groups: A longitudinal study.

Katerina Chin A Loy	PhD, UWA	N McClean M Robinson	How do early life family and social factors influence child's self-concept, body image and weight and shape concerns.
Dr Sunil Bhat	PhD, UWA	T Mori L Beilin	Familial determinants of cardiovascular risk factors among adolescents in a longitudinal Australian birth cohort, the Raine Study.
Elisha White	PhD, UWA	G Hall N De Klerk	Risk factors in the development of late-onset asthma in young adults: a longitudinal birth cohort study.
Esha Jamnadass	PhD, UWA	A Whitehouse, M Maybery	Investigating the relationship between cord blood estrogen and testosterone, and behavioural development.
Dr Anahita Hamidi	PhD, UWA	T Mori P Eastwood	Evaluation of cardio-metabolic risk factors in adolescents and young adults: impact on cardiac function and sleep respiratory events.
Amelia Stephens	PhD, UWA	A Whitehouse, M Maybery	The relation between rest-activity cycles and autistic-like traits
Tegan Grace	PhD, NDU	B Hands M Bulsara	A longitudinal analysis of factors impacting upon motor development during late childhood and adolescence.
Rob Waller	PhD, Curtin	A Smith P O'Sullivan L Straker	Cross sectional and longitudinal investigation of pain sensitivity in early adulthood.
Current Masters Students			
Hannah Forward	Masters UWA	D Mackey	Determinants of perfect vision: The Raine Eye Health Study, an ophthalmic follow up study of a longitudinal birth cohort for 21 years.
James Slater	Masters UWA	P Eastwood J Walsh L Straker	Assessing sleep using hip and wrist actigraphy.
Alex D'Vauz	Masters, Curtin	J McVeigh L Straker S Burns	The association between mental health, sleep and physical activity in young adults.
Laura Stockhill	Masters, Curtin	L Straker J Thompson	Uro-gynaecological symptoms: prevalence, severity, comorbidities, risk factors and impact in 22 year-old females
Amalia Bestry	Masters, ECU	T O'Sullivan T Mori	Nutritional determinants of cardiometabolic risk and mental health disorders from infancy to adulthood
Emily Omodei,	Masters, ECU	T O'Sullivan T Mori	Nutritional determinants of cardiometabolic risk and mental health disorders from infancy to adulthood
Current Honours Students			
David Moussa	Honours, UWA	P Eastwood A Mian K Shepherd	Craniofacial morphology and obstructive sleep apnoea.

Sophie Fleming	Honours, University of Queensland	A Whitehouse W Arnott	The Late Talking Population and Clinically Significant Autistic Traits
Overseas Students and Post Docs			
Edith van den Hoeven	Overseas Post Doc TKI	W Oddy RC Huang	Dietary patterns in relation to cardiometabolic health and bone mineral density in young Australians (Raine Study).
Romey Gaillard	Overseas Post Doc TKI	W Oddy RC Huang	Tracking of cardio-metabolic risk factors from early childhood into young adulthood.
Marieke Welton	Overseas student TKI	RC Huang, T Mori	Associations of maternal body mass index and weight gain during pregnancy with cardio- metabolic outcomes in adolescent offspring.
Stijn Hoogwout	Overseas Med Intern UWA	L Straker N McArdle	Musculoskeletal pain and restless leg syndrome in young adults
Natasja Lammers	Overseas Med Intern UWA	L Straker N McArdle	Restless leg syndrome in young adults from the Western Australian Pregnancy Cohort (Raine) Study.

Appendix 4: NEW NATIONAL AND INTERNATIONAL COLLABORATIONS 2015

1. Raine Study Asthma Group with La Trobe University, The University of Melbourne, Monash University and The University of Sydney to form a longitudinal analytical study of multiple cohorts in different regions of Australia.
2. Raine Study Developmental and Genetic Groups with Department of Human Genetics and Department of Psychiatry, Donders Institute for Brain, Cognition and Behaviour, Centre for Neuroscience, Radboud University Medical Center, Netherlands to replicate the top 21 genetic variants found by this Neuroscience group using data generated in a GWAS on autistic-like traits in the Raine cohort.
3. Raine Study Developmental Group with researchers from the Erasmus University in Holland to undertake a pooled analysis from two population-based cohort studies in Rotterdam (Generation-R) and Perth (Raine) to determine associations between growth in prenatal head circumference and autistic traits in the general population.
4. Raine Study Developmental Group and the speech pathology centre at University of Queensland to examine long-term language and cognitive outcomes of late-talking children.
5. Raine Study Developmental Group with the Queensland Brain Institute, University of Queensland as part of the National Autism CRC, utilising the Raine Study offspring as a control group.
6. Raine Study Eating Disorders Group with an established eating disorders researcher at the University of Texas, Austin, USA, and Oregon Research Institute for further expertise.
7. Raine Study Epigenetics Group with the Centre for the MRC Lifecourse Epidemiology Unit, University of Southampton, UK, to replicate epigenetic findings between the Raine Study and Southampton Women's Survey.
8. Raine Study Gastroenterology Group with Chief of Paediatric Gastroenterology, University of California, San Diego to provide expertise in inflammasome biology in relation to the association between inflammasome genetic polymorphisms and systemic and hepatic markers of inflammation.
9. Raine Study Genetic Group with University of Bristol to undertake a meta analysis to examine effect of maternal smoking on offspring adiposity using Mendelian Randomisation.
10. Raine Study Genetic Group with NIA, Harbor Hospital, Baltimore, USA to undertake a meta analysis of genome-wide association study of macronutrient intake.
11. Raine Study Genetic Group with University of Lausanne Department of Medical Genetics to perform meta-analysis of anthropometric traits.
12. Raine Study Genetic Group with the Department of Nutrition, Harvard School of Public Health, Boston USA to be part of a collaborative Mendelian Randomisation study investigating the association between dairy consumption and blood pressure and body mass index.
13. Raine Study Mental Health Group with Department of Child and Adolescent Psychiatry and Psychotherapy, University Medical Centre, Germany, which will involve specific and high

expertise as regards relevant statistical approaches (GMM), developmental aspects of psychopathology across different psychological disorders in children, adolescents and adults.

14. Raine Study Musculoskeletal Group with the Department of Anaesthesia and Pain Medicine, Sydney Children's Hospital, and a medical intern from University of Groningen in the Netherlands in a collaborative project focussing on pain and restless leg syndrome and the influence of iron levels and iron deficiency.
15. Raine Study Nutrition Group with the Centre of Excellence in Youth Mental Health, The University of Melbourne for specific expertise in fatty acids and youth mental health in relation to the nutritional determinants of cardio-metabolic and mental health risk.
16. Raine Study Ophthalmology Group with RMIT University in Melbourne to utilise an automated system for measuring retinal vessels in previously collected retinal scans.
17. Raine Study Reproductive Group with the Robinson Institute at the University of Adelaide to provide expertise on the evaluation of urine pregnanediol as a marker of ovulation and its association to reported menstrual cyclicity in adolescent girls.
18. Raine Study Sleep Group with the Appleton Institute, Central Queensland University for expertise in the field of shiftwork, fatigue and health collaborating on a project considering the effects of shiftwork on psychological and physiological parameters in young Australians.
19. Raine Study Vitamin D group with The Children's Hospital of Philadelphia who are undertaking a meta-analyses of the vitamin D GWAS.

Appendix 5: RAINE STUDY PUBLICATIONS 2015

1. Allen KL, Byrne SM, Crosby RD. Distinguishing between risk factors for bulimia nervosa, binge eating disorder, and purging disorder. *J Youth Adolesc.* 2015 Aug;44(8):1580-91.
2. Anderson D, Fakiola M, Hales BJ, Pennell CE, Thomas WR, Blackwell JM. Genome-wide association study of IgG1 responses to the choline-binding protein PspC of *Streptococcus pneumoniae*. *Genes Immun.* 2015;16(5):289-96.
3. Appannah G, Pot GK, Huang RC, Oddy WH, Beilin LJ, Mori TA, Jebb SA, Ambrosini GL. Identification of a dietary pattern associated with greater cardiometabolic risk in adolescence. *Nutr Metab Cardiovasc Dis.* 2015;25(7):643-50.
4. Atkinson HC, Marsh JA, Rath SR, Kotecha RS, Gough H, Taylor M, Walwyn T, Gottardo NG, Cole CH, Choong CS. Increased body mass index during therapy for childhood acute Lymphoblastic Leukemia: a significant and underestimated complication. *Int J Pediatr.* 2015; 386413.
5. Ayonrinde OT, Olynyk JK, Marsh JA, Beilin LJ, Mori TA, Oddy WH, Adams LA. Childhood adiposity trajectories and risk of nonalcoholic fatty liver disease in adolescents. *J Gastroenterol Hepatol.* 2015;30(1):163-71.
6. Bhat SK, Beilin L, Robinson M, Burrows S, Mori T. Contrasting effects of prenatal life stress on blood pressure and body mass index in young adults. *J Hypertens.* 2015;33(4):711-9.
7. Black LJ, Allen KL, Jacoby P, Trapp GS, Gallagher CM, Byrne SM, Oddy WH. Low dietary intake of magnesium is associated with increased externalising behaviours in adolescents. *Public Health Nutr.* 2015;18(10):1824-30.
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