Centre for Clinical Research in Neuropsychiatry
Report 2011—2012
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Report 2011—2012
CCRN Mission and Objectives

- To create and sustain in Western Australia an academic centre of excellence for multidisciplinary research in psychiatry and the neurosciences

- To generate scientifically valid databases and conduct advanced research into the aetiology of mental disorders, their management and treatment

- To provide research training and supervision of trainee psychiatrists; medicine, psychology and science students (graduate and postgraduate); and other mental health professionals

- To promote, facilitate and assist high-quality psychiatric, mental health and neuroscience research statewide, and especially within the WA mental health services

- To contribute towards informing and educating the community about the scientific understanding of mental disorders and the advances in their treatment and management
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Message from the Head of School of Psychiatry and Clinical Neurosciences, The University of Western Australia

During the year past, CCRN continued to be a centre of excellence in multidisciplinary neuropsychiatric research and I would like to thank the CCRN team for their hard work during 2012. The main focus of CCRN research remains on biomarkers and genetics of schizophrenia and related psychotic disorders, for which the Western Australian Family Study of Schizophrenia is a uniquely rich resource. Its Director, Winthrop Professor Assen Jablensky has established fruitful collaboration with major international and national consortia, whose aim is the discovery of gene networks contributing to psychoses, such as schizophrenia. Particularly of note is the participation of CCRN in Psychiatric Genomics Consortium 2 and the Wellcome Trust WTCCC2 Consortium, as well as the continuing collaboration with the Australian Schizophrenia Research Bank (ASRB). I am pleased to see the University continuing to work closely with the North Metropolitan Health Service – Mental Health. A recent example of this collaboration was the Survey of High Impact Psychosis (SHIP), led by Research Professor Vera Morgan, Head of the School’s Neuropsychiatric Epidemiology Research Unit (NERU). The research team has now completed its field work within the North Metropolitan Health Area and the start of data analysis is forthcoming.

Special mention is due to several of the Centre’s staff. Firstly, Johanna Badcock was promoted to Research Professor within the UWA School of Psychology. Research Associate Professor Flavie Waters was the lead organiser of the 2012 Australasian Society for Psychiatric Research (ASPR) conference in Fremantle. The conference was attended by researchers and clinicians from across Australia and overseas, and the three days of presentations and discussion were a showcase of novel and exciting research findings. Alix Mellor, a PhD student supervised by Flavie Waters, received the best poster award at the ASPR conference. A special mention is due to the students placed within CCRN and their supervisors, without whom we would not be able to maintain the education and training standards that UWA excels in. Congratulations to Saruch Chhabra, winner of the APS College of Clinical Psychologists student prize, who completed her PhD project in 2012, and to Esha Jamnadass, who received first class honours – both supervised by Johanna Badcock. Congratulations also to first class honours recipient Jeremy Downie, supervised by Flavie Waters. Special mention also of Katrin Hanken from the University of Bremen in Germany, who was placed within the Centre and completed her Masters in 2012 receiving a first class result.

Finally, I am delighted that CCRN will continue hosting the UWA monthly Psychiatry Research Seminar presentations, which sustained during 2012 their high standard, with exciting topics, such as Professor Nikos Stefonis’ seminar on pharmacogenetics and its implications for the treatment of psychiatric disorders.

Winthrop Professor Aleksandar Janca
Head, School of Psychiatry and Clinical Neurosciences
The University of Western Australia
Writing the Director’s Report for the year 2012 leads me to reflect on the past decade and a half of the life of CCRN. A major event of 2012 was the submission and subsequent endorsement of our application to The University of Western Australia for a renewal of the mandate of CCRN as an academic research centre. The outcome was a resounding success: the Academic Council of UWA resolved “to approve the application to renew the Centre for Clinical Research in Neuropsychiatry for a five year period”, and noted that “the Centre is the WA leading centre for advanced multidisciplinary research into the aetiology, management and outcomes of severe mental disorders”. The process of writing the renewal application was an occasion to look back at CCRN’s track record over the years. Since its establishment in 1995 CCRN researchers have published 594 research articles in high-impact peer-reviewed journals; have been awarded 109 competitive national and international research grants to a total value of $21,197,755; trained and supervised 38 PhD, 10 Masters and 33 Honours students; and hosted 6 national and international research conferences, including the Australasian Schizophrenia Conference and the Australasian Society for Psychiatric Research. Clinical and genetic researchers involved in the WA Family Study of Schizophrenia have discovered, characterised functionally and published 7 novel schizophrenia genes; examined in depth the so-called first rank symptoms of the disorder; investigated visual information processing and brain bioelectrical responses to stimuli; and applied sophisticated statistical modelling to integrate multiple neurocognitive measures into continuous phenotypic traits.

None of this would have been possible without the enthusiasm and dedicated work of CCRN researchers, all the way from the recruiting and interviewing of study participants to laboratory bench work, processing and analysing huge databases, employing complex paradigms to tackle specific hypotheses, and finally disseminating the results via print and oral word. And, of course, none of this would be possible without the willingness of patients, family members and other people in the community to contribute time and effort to research that will ultimately benefit those at risk for serious disorders of mind and body. However, it is often frustrating that the big aim of fully understanding exactly what and how goes wrong in a complex disorder like schizophrenia, and moreover developing the tools to prevent it from happening, is not yet within reach. We justifiably believe that what we are doing at CCRN leads us in the right direction to future knowledge, but we also owe the community research outcomes that can find application now. This is where the translation of research into viable clinical and behavioural practices becomes increasingly important and must be one of the key criteria for our self-evaluation.

A few examples will suffice. In 2012 we got from the WA Department of Health population databases complete information on the physical morbidity of WAFSS patients and their family members. Integrating this information into the individual data profiles of participants will enable us to understand better the relationship between mental disorder and physical disease and provide clues to preventative policies for the mental health services. The Diagnostic Interview for Psychoses (DIP), our main clinical tool, has attained wide recognition and popularity, both nationally and internationally. It has been translated into 7 languages and
adopted by researchers and clinical services in several countries. A major local undertaking was the initiation of an epidemiological survey within the North Metropolitan Health Services area by the UWA Neuroepidemiology Research Unit (NERU), affiliated with CCRN, as an extension of the National Survey of High Impact Psychoses (SHIP). It will provide vital clinical and social information, so much needed for the improvement of clinical care.

CCRN is now firmly embedded in the international and national collaborative network of research into the severe mental disorders. We are active members of large consortia, such as the Psychiatric Genomic Consortium 2 and the Wellcome Trust Consortium WTCCC2, as well as contributors to joint research with the Australian Schizophrenia Research Bank (ASRB) and with institutions in Indonesia, Mongolia, Norway, Vietnam and the USA. As of 2012 CCRN /WAFSS became a member of the Commonwealth Cooperative Research Centre for Mental Health (CRC-MH) with the mandate to develop and validate biomarkers for schizophrenia subtypes. CCRN researchers have been invited keynote speakers or presenters at a number of national and international conferences.

In conclusion, I wish to thank all researchers and supporting staff for their hard work and dedication to the values of CCRN, and to the success of our research program during 2012: (1) the WAFSS ‘coal face’ team of recruitment and assessment – Melanie Clark, Tammy Hall and Lisa Dawson, with assistance by Clea Louw, Sean Doyle, Emilia Janča and Maša Radević; (2) the exemplary NERU group, led by Vera Morgan and Anna Waterreus; (3) the ‘special expertise’ team including Milan Dragović, Johanna Badcock, Greg Price, Flavie Waters and Bharti Morar; (4) the Deputy Directors Dieter Wildenauer and Nikos Stefanis; (5) the PhD and Masters students who worked with us; (6) the many national and international experts whose comments and advice have left an imprint on our thinking; and, of course (7) the administrative assistance by Lorraine Bahri.

Winthrop Professor Assen Jablensky
Director, Centre for Clinical Research in Neuropsychiatry
External Links and Collaborations

International collaborations

Wellcome Trust Consortium WTCCC2 Cambridge, UK. Genetics of Endophenotypes in Schizophrenia. WAFSS cohort genotyped for genome-wide association studies (GWAS); co-authorship in the first journal publication of results (A Jablensky, M Dragović, L Kalaydjieva, B Morar).

Collaborative Group for Multi-Centre Genetic Studies of Schizophrenia. Collaboration in genome-wide association studies (GWAS) leading to joint publications (D Wildenauer, A Jablensky).

Psychiatric Genomic Consortium 2: Collaboration in genome-wide association studies (GWAS) in the largest pooled sample of schizophrenia cases and healthy controls to date (A Jablensky, D Wildenauer, L Kalaydjieva).

International Consortium for Hallucination Research (F Waters, J Badcock).

Department of Psychiatry and Institute of Genetic Medicine, Johns Hopkins University, Baltimore, USA. Phenotype-genotype relationships in schizophrenia (A Pulver, D Avramopoulos, A Jablensky, M Dragović).


University of Manchester, UK. Obstetric complications in women with severe mental illness (K Abel, V Morgan, A Jablensky).

University of Tromsø, Norway. Validation of the Norwegian translation of the Diagnostic Interview of Psychosis (V Hansen, I Skre, A Jablensky, V Morgan).

University of Erlangen, Germany. (i) Gene identification and characterisation in schizophrenia using cohorts from Germany and Indonesia. (ii) Gene identification in heroin dependence in a sample from Western Australia (S Schwab, D Wildenauer, G Hulse).

University of Indonesia, Jakarta, Indonesia. Recruitment and ascertainment of a schizophrenia case-control sample from mental hospitals in Jakarta and Bogor (N Amir, H Heriani, Irmansyah, D Wildenauer).

University of Bergen, Norway. Neurophysiology of auditory hallucinations (K Hugdahl, J Badcock).

Reading University, UK. Collaboration on first-rank (passivity) symptoms (N Holmes, F Waters, J Badcock, M Martin-Iverson, K Graham, A Jablensky).

Mongolia National Centre for Mental Health, Ulaanbaatar, Mongolia. Translation of the Diagnostic Interview for Psychosis and replication of WAFSS research procedures (Nasantsengel, Oyunchimeg, Guljanatand, Sarantuya. (G Price, A Jablensky).

National and Kapodistrian University of Athens Medical School, Athens, Greece. Validation of Greek translation of the Diagnostic Interview for Psychoses (N Stefanis, A Jablensky).
Collaborations within Australia (interstate)

Australian National Survey of High Impact Psychosis (SHIP): Universities and mental health services in WA, NSW, QLD, SA, VIC. (Technical Advisory Committee chaired by V Morgan, including members from the five states).

Australian Schizophrenia Research Bank (ASRB): CCRN was a founding member in this national collaboration, supported by NHMRC and involving collection of phenotype and neuroimaging data, as well as biological samples for genetic research (V Carr, A Jablensky, M Dragović et al.).

Cooperative Research Centre for Mental Health: A Commonwealth and industry-supported collaboration, including research groups in Melbourne and Perth (A Jablensky, N McCarthy and WAFSS team).

Queensland Brain Institute and University of Queensland: Genome-wide association analysis of the Western Australian Family Study of Schizophrenia, WAFSS (N Wray, P Visscher, A Jablensky, L Kalaydjieva).

Queensland Brian Institute and University of Queensland: Conducting statistical and bioinformatics analyses of the Indonesian case/control sample (B Benyamin, N Wray, D Wildenauer)

University of Queensland. Environmental risk factors for schizophrenia: Workshop of J McGrath with research staff of the Neuroepidemiology Research Unit (V Morgan et al.).

University of Newcastle, NSW. Spatial Working Memory in Schizophrenia and the effects of nicotine. PhD project. (J Todd, A Barker, V Clark).


Collaborations within Western Australia

School of Psychology, The University of Western Australia. Visual processes in autism. (D Badcock, M Maybery, J Badcock)

School of Psychology, The University of Western Australia. Attitudes of psychology students to mental illness (C Lawrence, J Badcock)

Centre for Genetic Origins of Health and Disease, The University of Western Australia. Exome sequencing of 88 WAFSS families with schizophrenia (E Moses, N McCarthy, P Melton, A Jablensky, B Morar, J Badcock)

Institute for Child Health Research.: Environmental risk factors and developmental pathways in schizophrenia (C Bower, S Zubrick, V Morgan, A Jablensky).

Centre for Sleep Sciences, School of Psychology, The University of Western Australia; The Marian Centre, Perth: Collaboration on sleep disorders (P Eastwood, R Bucks, M Ree, F Waters).

Crime Research Centre, The University of Western Australia. Offending patterns and psychiatric illness (F Morgan, A Ferrante, V Morgan).

Department of Health of Western Australia. Long-term outcomes of early intervention in psychosis (G Smith, T Williams, V Morgan)
Current Research Projects

Western Australian Family Study of Schizophrenia (WAFSS)

A Jablensky, J Badcock, M Dragović, G Price, N Stefanis, V Morgan, B Morar, F Waters, M Clark, T Hall

The core aim of WAFSS since its inception in 1996 has been to assess the phenotypic and genetic heterogeneity of schizophrenia by subtyping the clinical disorder based on objectively measurable endophenotypes and ‘deconstructing’ its phenotype into component cognitive and neurophysiological syndromes with characteristic genetic underpinnings. By the end of 2012 the WAFSS cohort comprised 1262 individuals (533 with schizophrenia, 397 family members and 332 healthy controls). It includes 133 nuclear families, each with a schizophrenia proband; and 328 first-degree family members of whom 145 have been diagnosed with schizophrenia spectrum or other psychiatric disorders. Clinical assessment includes a diagnostic interview and best-estimate diagnoses (ICD-10 and DSM-IV). Neurocognitive assessment involves 12 tests targeting general ability (premorbid and current IQ); verbal learning and memory; executive function; verbal fluency; sustained attention; speed of information processing; psychometric measures of schizotypy; and a neurological examination of ‘soft’ neurological signs. The phenotype is complemented with electrophysiological measures (event-related potentials). In constructing endophenotypes for genetic analyses the neurocognitive and personality measures are aggregated into quantitative traits using latent structure analysis. Additional information on maternal obstetric complications and physical morbidity of the probands and their family members was obtained in 2012 from WA population health databases and added to the phenotype profiles. We have at present highly enriched phenotypes for genomic studies: (i) clinical symptoms and diagnosis; (ii) neurocognitive profiles; and (iii) physical comorbidity and maternal obstetric history. DNA, RNA, serum and plasma samples from the cohort, as well as lymphoblastoid cell lines, are stored at the WA DNA Bank. Our findings to date support the utility of parsing the broad phenotype of schizophrenia into component endophenotypes that reduce heterogeneity and enable the capture of informative genetic variation. Genetic analyses of WAFSS have revealed two novel candidate genes (NRN1 and LYRM4) which were characterised by functional studies and bioinformatics. Another finding was the involvement of the Reelin signalling cascade in cognitive deficit in schizophrenia, raising the hypothesis of accelerated brain aging in the subset of cases characterised by pervasive cognitive deficit (CD). Participation of WAFSS in large international consortia contributed to the discovery of five new schizophrenia loci (published in Nature Genetics 2011;43: 969–976) and of a common variant at chromosome 16p11.2 conferring risk of both schizophrenia and bipolar disorder. In 2012 we sequenced the exome of the metabotropic glutamate receptor 1 (mGluR1) in 450 patients and 605 controls and detected deleterious mutations in schizophrenia cases and in family members with diverse psychiatric and neurological conditions, including Asperger syndrome, depression and epilepsy, suggesting a pleiotropic contribution to a spectrum of morbidity. The next step in this research will involve a whole exome sequencing of the WAFSS families.
Pathways of risk from conception to disease: a population-based study of the offspring of women with schizophrenia, bipolar disorder and other psychotic disorders

V Morgan, A Jablensky, G Valuri, M Croft, J Griffith, S Shah, P Di Prinzio, S Zubrick, C Bower, T McNeil, D Young, F Morgan

This is a whole-of-population record linkage epidemiological study employing a developmental perspective to examine risk factors affecting the reproductive health of women with severe mental illness and to conduct a ‘virtual’ follow-up of the development and neuropsychiatric sequelae in their offspring. Children at increased familial risk for severe mental illness are compared with children at no increased familial risk on a wide range of developmental indices and environmental risk factors, including obstetric events, with a view to elucidating the intergenerational transmission of both vulnerability and resilience to adverse neuropsychiatric outcomes. These outcomes include, among others, birth defects, intellectual disability, pervasive developmental disorders, epilepsy, and psychiatric illness including psychosis. We use linkage across psychiatric, physical morbidity, mortality and other administrative registers in Western Australia to follow up a large cohort of all 467,945 children born between 1980 and 2001 to 246,874 mothers. This includes 15,486 births to 7508 mothers with a psychotic illness. In the course of the study we have developed or refined a number of instruments, including the Diagnostic Interview for Psychoses (casenotes version) and the Children’s Checklist; extended the McNeil-Sjöström Scale for Obstetric Complications; and designed indices of neonatal encephalopathy and of maternal morbidity over time. We are also developing measures of adversity across individual, familial and ecological settings using record-linked data. Using quantitative and qualitative data, we are constructing developmental life course histories for the children in our study, examining the following outcomes: maternal reproductive morbidity and early neonatal morbidity; stillbirths, perinatal and childhood mortality; sudden infant death syndrome; early neuropsychiatric outcomes including birth defects, intellectual disability and rare syndromes; education outcomes; childhood victimisation (using prospectively collected child protection data); and criminal offending. In work in progress, the children’s mental health outcomes are being reviewed. We are working towards our flagship paper that will examine familial and environmental risks for psychosis in these high risk children of mothers with psychosis.

Intellectual disability and other neuropsychiatric outcomes in high-risk children of mothers with schizophrenia, bipolar disorder and unipolar major depression

V Morgan, M Croft, G Valuri, S Zubrick, C Bower, T McNeil, A Jablensky

This study used the data collected as part of the project on Pregnancy, Delivery, and Neonatal Complications in a Population Cohort of Women with Schizophrenia and Major Affective Disorders. The aims of this study were: (a) to determine the risk of intellectual disability, rare syndromes, pervasive developmental disorders, convulsions and epilepsy in a population-based cohort of children of women with schizophrenia compared with children of women with no recorded psychiatric history; (b) to examine the role of obstetric complications in mediating the risk of intellectual disability; and (c) to assess the specificity of findings to maternal schizophrenia compared with maternal bipolar disorder and unipolar major depression. Our findings provide epidemiological support for clustering of neuropsychiatric disorders in children of women with psychotic illness. Children were at significantly increased risk of intellectual
disability with odds ratios (ORs) of 3.2 (95% CI 1.8–5.7), 3.1 (95% CI 1.9–4.9) and 2.9 (95% CI 1.8–4.7) in the maternal schizophrenia, bipolar disorder and unipolar depression groups respectively. Multivariate analysis suggests familial and obstetric factors may contribute independently to the risk. Although summed labour/delivery complications (OR = 1.4, 95% CI 1.0–2.0) just failed to reach significance, neonatal encephalopathy (OR = 7.7, 95% CI 3.0–20.2) and fetal distress (OR = 1.8, 95% CI 1.1–2.7) were independent significant predictors. Rates of rare syndromes in children of mothers with mental disorder were well above population rates. Risk of pervasive developmental disorders, including autism, was significantly elevated for children of mothers with bipolar disorder. Risk of epilepsy was doubled for children of mothers with unipolar depression.

**Association studies in a large case/control sample with schizophrenia from Indonesia**

D Wildenauer, S Schwab, Nan Dai, WenWen Qin, AAA Kusumawhardani and Indonesian Schizophrenia Genetics Consortium

In collaboration with the Department of Psychiatry in Jakarta we have ascertained a sample of 1117 cases with schizophrenia and 1148 non-psychiatric controls and prepared genomic DNA. The recruitment involved patients from five major mental state hospitals in the area of Jakarta and was conducted by local psychiatrists (clinical interviews using the Indonesian version of the Diagnostic Interview for Psychoses, DIP) and nurses (organisation and blood withdrawal). We used a panel of 374 SNP markers from Illumina for cleaning, identifying and eliminating samples with poor DNA quality; duplications (double sampling, errors in labelling, identical twins, etc), and ethnical outliers. The sample is being used for association studies testing potential susceptibility loci. We have obtained evidence for association of SNP rs1344706, located in an intron of ZNF804 on chromosome 2q32.1, and first published by O’Donovan et al (2008) in a genome-wide association study. We have been able to confirm this association in the Indonesian family sample. We have also tested selected SNPs from published GWAS studies. Out of 4 SNPs in the regions of TCF4 (18q21.2), MIR137 (1p23.3), NT5C2 (10q24.33) and CSMD1 (8p23.2) respectively, which were GWAS significant in Caucasian samples, rs10503253 located in the CSMD1 region produced a P = 0.009 in the case control and 0.03 by TDT in the family sample. We tested eight SNPs located in the MHC region (6p21-6p22.1) in the currently available case control sample from Indonesia and obtained P = 0.019 for rs2142731 and P = 0.06 for rs1635. Dependent on funding, we are planning to expand the sample to at least 2000 cases and 2000 controls and explore the HLA region on chromosome 6 for association.

**The 2010 Australian National Survey of High Impact Psychosis (SHIP)**

V Morgan, A Jablensky, A Waterreus, J Griffith, Patsy Di Prinzio, Sonal Shah

The aims of this epidemiological survey were (i) to describe the prevalence and profiles of psychotic disorders in Australia and (ii) to identify factors associated with good outcome in psychosis that are amenable to change and critical to recovery with the intention of informing policy development and service planning. The survey is an initiative of psychosis researchers and clinicians across Australia in partnership with the Australia Government Department of Health and Ageing. It is a follow-up to the first Australian National Survey of Low Prevalence
(Psychotic) Disorders, conducted in 1997-98 by Prof Assen Jablensky and teams of investigators who collected national data that provided an evidence base for understanding barriers to good outcomes for people with psychosis, including their social and economic integration. SHIP interviews ask questions about: symptoms, utilisation of mental health and other services; perceived need; education; cognition; social participation (work and skill development; activities of daily living; family responsibilities; other social engagement and community integration); living circumstances; support networks; physical well-being (including a physical health assessment; physical activity; nutrition; risk factors for metabolic syndrome and cardiovascular disease; smoking); and drug and alcohol use. The SHIP study took place at seven sites in five states across Australia: NSW, QLD, SA, VIC and WA, using a two-phase sampling design. Phase 1 (screening for psychosis) took place in the census month of March 2010. In Phase 2, 2000 individuals aged 18-64 were randomly selected for participation from those screen-positive for psychosis, to be interviewed and assessed. The interview phase was completed at the end of 2010. The report to the Australian Government Department of Health and Ageing was completed in 2011 and the first series of papers, including an overview paper, was published in 2012. Papers from this study are available for downloading at: http://www.psychiatry.uwa.edu.au/research/neru/survey/researchers

North Metropolitan Area Survey of High Impact Psychosis (North Metro SHIP)

V Morgan, A Waterreus, J Griffith, A Jablensky, Patsy Di Prinzio, Sonal Shah

This extension of the national SHIP survey in North Metropolitan Area Health Services Mental Health was funded by the Mental Health Commission and the Western Australian Department of Health. The survey census month was March 2012 with interviews taking place from April 2012 to April 2013. The aims were to: (i) estimate the prevalence of psychoses in North Metropolitan Area Health Service; (ii) describe the social and economic circumstances of people living with psychosis within North Metro, as well as their mental and physical health profiles and their use of services; (iii) develop a local evidence base to help inform mental health policy development and service providers in North Metro; and (iv) develop services to meet specific local needs to benefit people living with psychosis, their friends, family, carers and services supporting them.

Schizophrenia and criminal offending: A whole-of-population study of the prevalence and patterns of criminal offending in people with schizophrenia and other psychiatric disorders

V Morgan, F Morgan, G Valuri, A Ferrante, D Castle, A Jablensky

This study employs a methodologically sound, population-based research design to provide reliable data on the association between offending and serious mental illness. Its aims were: to (i) estimate the prevalence of offending in people with a mental illness compared to the general population; (ii) to describe patterns of offending in people with a mental illness compared to the general population; and (iii) to compare findings for people with schizophrenia with those with other mental illness. The vast majority (89%) of offenders arrested between 1986 and 1996 did not have a mental illness. Eighty percent of those arrested for a violent offence did not have a mental illness; 6% had a substance abuse disorder; 2% had a personality disorder and only 2%
had schizophrenia. Seventy percent of those arrested for homicide in the same period did not have a mental illness, 9% had a substance abuse disorder, 3% had a personality disorder and 3% had schizophrenia. Among people with a mental illness, the prevalence of offending over a 12 year period from 1986-1996 was 32% overall. The prevalence was differentially distributed, depending on diagnosis, and was highest for substance abuse disorders (59%). The prevalence for schizophrenia was 39%. A comorbid substance abuse disorder significantly increased the risk of a violent offence for people with schizophrenia. For the majority of offenders with a mental illness, their first arrest preceded their first contact with mental health services. This proportion had increased to 66% over time for people with schizophrenia. The annual change in the number of arrests over a 12 year period from 1986-1996 for the cohort born 1955-1969 decreased significantly for people with no mental illness and increased significantly for those with a mental illness other than schizophrenia. There was no overall change for people with schizophrenia but there was a peak in the pattern of arrests in 1991-1993, coinciding with a period when community mental health services were poorly resourced to meet demands created by deinstitutionalisation of patients from psychiatric institutions. Papers from this study are available for downloading from:

**Understanding auditory hallucinations**

J Badcock, M Maybery

The aim of this ongoing series of projects is to understand the cognitive, biological and emotional processes causing auditory hallucinations. This research has uncovered differences and similarities in the experience of auditory hallucinations in schizophrenia and ‘hearing voices’ in the general community, and has shown that poor emotion regulation increases hallucination frequency, and that perception of voice identity differs in patient and non-patient voice hearers. Each of these findings has important implications for treatment. The current project aims to examine whether people with hypomanic personality traits have a tendency to hallucinate and, if so, what mechanisms are involved.

*Related Honours and PhD projects:* Hallucinations and mild hypomania (S Mahfouda, Hons, School of Psychology).
**Visual processing in autism**

J Badcock, D Badcock, M Maybery

Autism spectrum disorders (ASDs) include Autistic Disorder, Asperger's disorder and pervasive developmental disorder. ASDs are developmental disabilities characterised by impairments in social interaction and communication, and restricted, repetitive interests, activities and behaviours. Alongside these difficulties individuals with ASDs or high levels of autistic-like traits show superior performance on visual search tasks compared to typically developing controls. The aim of this research is to understand the mechanisms underlying this visual skill and to develop a new, more reliable visual search task that will improve the clinical assessment of ASDs.

*Related Honours and PhD projects:* Visual search and Autism. H Mighall, DPych. School of Psychology); Development of Global Processing of Visual Stimuli in Autism Spectrum Disorders. S Cribb (PhD, School of Psychology).

**Attitudes of mental health professionals to mental illness**

J Badcock, C Lawrence

Negative attitudes to mental illness are not limited to members of the general community: recent evidence indicates that people with mental illness often feel negatively stereotyped and dehumanized by mental health professionals. It is currently unknown if negative attitudes to mental illness develop following professional training [e.g. due to burnout], or are already present in students intending on a career in mental health. This project aims to assess these issues and will guide the training of future mental health professionals.

*Related Honours and PhD projects:* Attitudes to mental illness in psychology students. M Hofmeester (Hons, School of Psychology)

**Collaborative psychosis research in Mongolia**

Dr Nasantsengel, Dr Oyunchimeg, Dr Guljanat (NCMH). Dr Sarantuva (Health Sciences University, Mongolia); G Price, B Morar (CRC/CCRN); A Jablensky (CCRN).

The project is a collaboration with the National Centre of Mental Health, Mongolia (NCMH). The aim of the project is to assist colleagues in Mongolia to develop a state-of-the art study of psychotic disorders by adapting methodological aspects of the Western Australian Family Study of Schizophrenia (WAFSS). In 2011-2012 the Diagnostic Interview for Psychoses (DIP) was translated into Mongolian and two psychiatrists from NCMH visited CCRN for training in research procedures. Additional research procedures, including electrophysiological assessment and collection of blood samples for DNA extraction and genetic analyses are underway. The NCMH manages the project in Mongolia and is the Chief Investigator Unit, with CCRN and the Clinical Research Centre (CRC) as partners.
Western Australian Family Study of Schizophrenia: ERP endophenotype (MMN) analysis with hallucinations.

J Badcock, G Price, P Michie

This project utilises the WAFSS dataset to test the hypothesis of an auditory system basis for auditory hallucinations. In addition, it seeks to incorporate complementary neurocognitive data as a potential factor in this model. Specifically, we expect that a particular profile of electrophysiological endophenotypes associated with the auditory system will differ in schizophrenia patients reporting auditory hallucinations from patients with no hallucinations, from their well relatives, and from normal controls. Analysis will be conducted using profile analytic techniques, sequential regression, and Dynamic Casual Modelling.

International collaborative projects on schizophrenia genetics

D Wildenauer, S Schwab

This collaboration involved a SNP-genome scan in samples from 8 centres including 971 families with schizophrenia (102 families from Germany were contributed by our group). Altogether, 4540 subjects (2120 affected) have been genotyped for 5955 SNPs (CIDR/Illumina). Follow-up on a linkage scan by GWAS, genotyping 544,131 SNPs, was submitted for publication in the American Journal for Psychiatry. In addition, this sample has been included into a large collaboration with more than 50,000 subjects, performing a GWAS with 1.2 mln SNPs. This collaborative genome-wide association study identified five new schizophrenia loci and was published in Nature Genetics 43: 969–976, 2011.

PIPKIIa, a candidate gene for schizophrenia: the impact of DNA polymorphisms on gene and protein expression and function

D Wildenauer, S Schwab, L Saggers-Gray

The aim of this project was to follow-up a candidate gene for schizophrenia, PIPKIIa. We have identified this gene as being located in a schizophrenia linked region on chromosome 10p. In addition, association with DNA sequence variants located in this gene was demonstrated by our group. Analysis of associated DNA variants in a sample of 152 sib-pair families obtained in collaboration with Dr Irmansyah at the University of Indonesia in Jakarta is now completed. Further we studied gene expression and impact of DNA sequence variants on expression levels. Currently we are investigating a potential functional variant in the gene by cloning the two isoforms and testing for efficiency in phosphorylation of the substrate PIP2.
The Australian perinatal mental health reforms: using population data to evaluate their impact on service utilisation and related cost-effectiveness

M-P Austin, E Sullivan, N Hight, V Morgan, C Mihalopoulos, M Croft, K Brameld (in partnership with beyondblue).

Mental health problems associated with the perinatal period – defined as from conception to the end of the first postnatal year – are recognised as a major public health issue with significant morbidity and costs for mother, infant, and family. Left untreated they may impact on the health of the next generation. The last decade has seen a burgeoning of perinatal mental health initiatives in Australia, including the National Perinatal Depression Initiative (NPDI), yet there is currently a gap in our understanding of how these initiatives have met their goal of improving maternal mental health outcomes through improved uptake of services, at this critical time. This project is using population health data to examine the impact of the reforms on maternal health outcomes, service utilisation and the likely cost-effectiveness of these reforms. It employs four key methodologies: (i) data linkage; (ii) generation of perinatal-specific Medicare Benefits Schedule summary data; (iii) economic and policy analyses; and (iv) key stakeholder consultations in a consideration of the further implementation and evaluation of the Depression Initiative NPDI. The findings will facilitate improvements in the recognition, prevention, and treatment of mental morbidity among perinatal women. It will provide information for the provision of effective mental health services to this vulnerable (and eminently accessible) population. The project will empower beyondblue, as its partner organisation, to use the findings to strengthen collaborations, advocate for a cohesive approach to the future implementation of the NPDI, and influence policy and decision making at jurisdictional and national levels. From an international perspective, this project will put Australia at the forefront of policy planning, analysis and cost-effectiveness evaluation in the field of perinatal mental health.
Research Grants

New Grants

Overcoming barriers to improved physical health in people with severe mental illness. National Health and Medical Research Council Project Grant. V Morgan, A Jablensky, G Watts, J Badcock, K Cox, N Stefanis.
$830,470

$310,000

Does manipulation of arterial sheer stress enhance cerebrovascular function and cognition in the aging brain? National Health and Medical Research Council Project Grant. D Green, N Lautenschlager, K. Cox, J Badcock.
$684,689.27

Contract to extend the North Metropolitan Survey of High Impact Psychosis. V Morgan.
$167,625

Contract to fund Part 1 of Long-Term Treatment Outcomes in Early Psychosis Specialist Services. WA Mental Health Commission (paid to WA Mental Health Policy Research Centre). T Williams, G Smith, V Morgan, D Young.
$196,412

US$176,040

Continuing Grants

Memory, synaptic plasticity and gene networks in schizophrenia. National Health and Medical Research Council Project Grant 2008-2013
$1,126,782

$1,009,800

$770,476
Honours and Postgraduate Research

Honours students

Completions


In Progress

Madeleine Hofmeester. School of Psychology, The University of Western Australia. Attitudes to mental illness in psychology students. Supervisors: J Badcock, C Lawrence.

Simone Maftouda. School of Psychology, The University of Western Australia. Hallucinations, inhibition and hypomanic personality. Supervisors: M Maybery, J Badcock.


Masters Students

Completions

Katrin Hanken (student placement from Bremen University). Sleep-disordered breathing in schizophrenia. Supervisor: F Waters. Awarded first-class degree.

In Progress

Devon Spaapan. Examination of emotion regulation mechanisms in subclinical symptoms of psychosis. Supervisor: F Waters.
Doctoral Students

Completions


In Progress


Michelle Hodge. Sleep disturbances and behavioural and psychiatric symptoms of dementia. Supervisors: F Waters, R Bucks.


Serena Cribb. Development of global processing of visual stimuli in autism spectrum disorders, PhD. School of Psychology, The University of Western Australia. Supervisors: D Badcock, M Maybery, J Badcock.


Publications

Journal Articles


Waters F. (2012). Editorial theme introduction: Multidisciplinary approaches to understanding auditory hallucinations in schizophrenia and non-schizophrenia and non-schizophrenia populations (The International Consortium on Hallucination Research). *Schizophr Bull* 38; 693-4.


**Books and Chapters**


Conference, Seminar and Workshop Presentations

Oral Presentations


Bose A. Bilateral visual impairment of non-ocular causes - a profile. The Association of Physicians of India Conference (APICON) held in Kathmandu, Nepal. Published in The Journal of the Association of Physicians, India (JAPI); 43, p 916.


Jablensky A. Mental health 2020: challenges and opportunities. Invited presentation. European Network of Mental Health Service Research (ENMESH), Ulm, Germany, June 2011.


Jablensky A. Training workshop on the Diagnostic Interview for Psychoses (DIP), Department of Psychiatry, University of Tromsø, Norway, October 2012.


Morgan V. A profile of Australians with psychosis. Findings from the 2010 Australian National Survey of High Impact Psychosis (SHIP). *The University of Western Australia School of Psychology Colloquium*, May 2012.

Morgan V. People living with psychotic illness in 2010 and the North Metro Survey of High Impact Psychosis (SHIP). North Metropolitan Area Health Service Mental Health: *Mental Health Executive Group*, March 2012.


Morgan V. The Pathways Study: The potential of data linkage as a research tool for discovery and applications. *Centre for Clinical Research in Neuropsychiatry Seminar Series*, July 2012.


Waters F. Cognitive processes associated with voice-hearing. Webinar on Auditory Hallucinations (moderator and speaker), Schizophrenia Research Forum,

Waters F. Sleep and depression in older adults (invited talk). North Metro Area Older Adult Mental Health Program, 2011.

Waters F. Sleep and psychiatry (invited talk). Telethon Research Institute, Perth, 2011.

Wildenauer DB. Schizophrenia susceptibility genes in the Indonesian population. 18th Annual Molecular Psychiatry Meeting, Park City, USA, February 2011.

Wildenauer DB. Schizophrenia susceptibility genes in the Indonesian population. Genemappers, Hobart, Australia, 2011.

Wildenauer DB. Investigation of schizophrenia susceptibility genes in the Indonesian population. WA Institute of Medical Research Seminar, 2011.


**Poster Presentations**


Price G, Bose A, Jablensky A. Interactions between genotype and EEG state affect electrophysiological endophenotype behaviour. 10th World Congress of Biological Psychiatry, Prague, 2011.


Wildenauer DB. A large sample of heroin addicted individuals from Western Australia treated with naltrexone implants for genetic and pharmacogenetic studies Genemappers 2011, Hobart, Australia, April 2011.

Wildenauer DB. Association of candidate genes conferring susceptibility to schizophrenia in a sample with 1097 cases and 1112 controls reveals association with rs1344706 located in the ZNF804A gene. 12th International Conference on Human Genetics & 61st Annual Meeting of the American Society of Human Genetics, Montreal, Canada, October 2011.

Wildenauer DB. Investigation of GWAS findings in schizophrenia in a case control and a family sample from Indonesia. 62nd Annual Meeting of the American Society of Human Genetics, San Francisco, USA, 2012.
Membership in International, National and State Committees

Badcock JC. Member, National Health & Medical Research Council, Centres of Research Excellence, Clinical Panel

Badcock JC. Member, National Health & Medical Research Council, Research Translation Faculty.

Badcock JC. Member, Schizophrenia Research Institute, Cognitive Neuroscience group.

Badcock JC. Member, Australian Psychosis Research Network.

Badcock JC. Member, Advisory and Liaison Committee, D/Psych training programme, School of Psychology, UWA.


Jablensky A. Chair, Scientific Program Committee for Perth 2014 Congress of RANZCP.

Jablensky A. Member, Scientific Advisory Committee of the Mental Health Research Institute (MHRI), Melbourne, VIC.

Jablensky A. Member, Steering Committee of Australian Psychosis Research Network (APRN).

Jablensky A. Member of Editorial Boards: Australian and New Zealand Journal of Psychiatry; British Journal of Psychiatry; Epidemiology and Psychiatric Sciences; International Review of Psychiatry; Psychological Medicine; Schizophrenia Bulletin.

Morgan V. Chair, National Survey of High Impact Psychosis (SHIP) Phase 3 Technical Advisory Group.

Morgan V. Chair, North Metro Survey of High Impact Psychosis (North Metro SHIP) Phase 3 Technical Advisory Group.

Morgan V. Committee member, Intellectual Disability Exploring Answers (IDEA) Advisory Council and Ethics Committee.

Morgan V. Executive Member, Australian Psychosis Research Network.

Morgan V. Member, National Health and Medical Research Council Grant Review Panel for Psychology / Psychiatry and Cognitive Sciences.


Waters F. (2012) External Interviewer, School of Psychology interview Board, The University of Western Australia


Wildenauer DB. Graduate Research Coordinator. School of Psychiatry and Clinical Neurosciences, The University of Western Australia.

Wildenauer DB. Member of the Faculty Scholarships and Fellowships Committee. Faculty of Medicine and Dentistry, The University of Western Australia.

Wildenauer DB. Member of the Faculty Strategic Research Advisory Group. Faculty of Medicine and Dentistry, The University of Western Australia.

Wildenauer DB. Member of the Higher Degrees Committee. Faculty of Medicine and Dentistry, The University of Western Australia.
The CCRN Team 2012 together with collaborating researchers from the NMHS-MH Clinical Research Centre

From left to right: Tammy Hall, Melanie Clark, Lisa Dawson, Emilia Janca, Vera Morgan, Maša Radević, Assen Jablensky, Milan Dragović, Bharti Morar, Flavie Waters, Joanna Badcock, Greg Price, Nikos Stefanis and Dieter Wildenauer.
Staff and students, 2011-2012

Jablensky, Assen. Winthrop Professor, School of Psychiatry and Clinical Neurosciences, UWA. Director, CCRN

Wildenauer, Dieter. Professorial Fellow, School of Psychiatry and Clinical Neurosciences, UWA. Deputy Director, CCRN

Morgan, Vera. Head, Neuropsychiatric Epidemiology Research Unit, School of Psychiatry and Clinical Neurosciences, UWA

Stefanis, Nikos. Professor of Psychiatry, Graylands Campus

Martin-Iverson, Mathew. Professor, School of Medicine and Pharmacology, UWA

Badcock, Johanna. Specialist Clinical Psychologist

Dragović, Milan. Senior Scientist (Neuropsychiatry)

Price, Greg. Senior Scientist, Neurophysiology

Stefanis, Nikos. Professor of Psychiatry, Graylands Campus

Waters, Flavie. Associate Professor / NHMRC Senior Research Fellow, School of Psychiatry and Clinical Neurosciences, UWA

Morar, Bharti. Laboratory Technician

Clark, Melanie. Research Officer (CCRN)

Hall, Tammy. Research Officer (ASRB)

Research Assistants
Sean Doyle, Emilia Janca, Maša Radević, Wen Wen Qin, Mutiara Wildenauer.
JABLENSKY Assen, MD, DMed Sc, FRCPsych (UK), FRANZCP
Winthrop Professor of Psychiatry, UWA
Director, CCRN

(08) 9347 6416
assen.jablensky@uwa.edu.au

Overall direction, planning and supervision of CCRN research; study design; clinical diagnostic assessments; phenotype analysis for genetic studies; genetic epidemiology; PhD supervision; liaison with sponsoring organisations and translational research. Having completed his medical degree and training as a psychiatrist in Bulgaria and the UK, Jablensky has worked as a researcher and clinician in Switzerland (WHO, Geneva, 1974-1986); Bulgaria, where he was Director of the National Program of Brain and Behaviour Research (1987-1992); President of the Medical Academy (1988-1992); and a Fellow at Stanford University, US (1992-1993). He moved to Australia in 1993. The main focus of his research is on psychiatric epidemiology, genetics, psychiatric classification and psychotic disorders. At WHO Geneva, Jablensky was Principal Investigator of the WHO Ten-Country Study on Schizophrenia and lead author of its report, which remains among the most widely quoted papers in the psychiatric literature. During 1982-1987 he chaired the WHO Task Force which developed the ICD-10 diagnostic criteria for mental disorders. In Australia, Jablensky was Project Director of the National Study on Low-Prevalence (Psychotic) Disorders (1997-1998) and Chief Investigator on multiple National Health and Medical Research Council and US research grants. Jablensky is Associate Editor of the British Journal of Psychiatry, Schizophrenia Bulletin and Psychological Medicine, and member of the Editorial Boards of International Review of Psychiatry, the Australian and New Zealand Journal of Psychiatry and Epidemiology and Psychiatric Science. He has over 300 publications (h-index: 45), of which currently 165 are articles in peer reviewed research journals and over 100 are book chapters and books. Jablensky has been awarded the Strömgren Prize for psychiatric epidemiology; the ASPR Founders Medal, the Organon Research Prize, and the Honorary Fellowship of the Royal College of Psychiatrists (UK). At present, Jablensky is Director of the Centre for Clinical Research in Neuropsychiatry (The University of Western Australia), and Consultant Psychiatrist at the Royal Perth Hospital.
CLARK, Melanie, BSc (Hons) (Psychology)
Research Officer

(08) 9347 6798
melanie.clark@health.wa.gov.au

Coordination of WAFSS and ASRB research activities, assessment of research volunteers (patients and controls), administration of neuropsychological and neurological tasks and clinical interviews, data entry, report writing, data analysis, participant reimbursement.

DAWSON, Lisa BSc(Hons) (Psychology)
Research Officer

(08) 9347 6502
lisa.dawson@health.wa.gov.au

Maintenance of research databases; training new staff and administration of neuropsychological tasks and clinical interviews.

DOYLE, Sean
Research Officer

(08) 9347 6415
sean.doyle@uwa.edu.au

Conducting initial telephone interviews of potential participants before coming in for testing. Data linkage, creation of frequency tables and creating individual timeline spreadsheets of WAFSS participants.

HALL, Tammy, BSc (Psychology)
Clinical Assessment Officer

(08) 9347 6415
tammy.hall@health.wa.gov.au

Recruitment and assessment of volunteers for the ASRB project; assessments include cognitive, neurological and clinical interviews. Organises and attends participant MRI scans. Data entry, report writing and liaison with colleagues.
JANCA, Emilia
Research Assistant

(08) 9346 6429
emilia.janca@uwa.edu.au

Identification of families for potential recruitment and classification of those in order of priority. Creation of database through data linkage.

MORGAN, Vera
Operational Epidemiologist, CCRN

(08) 9346 6439
vera.morgan@health.wa.gov.au

Professor Vera Morgan is Head of the Neuropsychiatric Epidemiology Research Unit in the School of Psychiatry and Clinical Neurosciences at The University of Western Australia and Operational Epidemiologist at CCRN. She is a psychiatric epidemiologist with a special interest in the epidemiology and aetiology of schizophrenia and other psychotic disorders, using both record-linkage methodology and survey methods. She was Convenor of the Technical Advisory Group for the National Project of the Survey of High-Impact Psychiatric Disorders (SHIP). Her professional roles have included: President, Australasian Society for Psychiatric Research; Vice-President: Australasian Epidemiological Association; Chair: Research Committee of the Mental Health Council of Australia; and Member: The University of Western Australia Senate.

RADEVIC, Masa
Graduate Research Assistant

(08) 9346 6429
masa.radevic@uwa.edu.au

Recruitment of controls and probands. Conducting initial telephone interviews of research subjects. Assisting with data entry and database management. Participating in quality improvement and internal audit activities.
WILDENAUER, Dieter
Professorial Fellow, Deputy Director of CCRN

(08) 9347 6782
wildenauerd@meddent.uwa.edu.au

Institutional liaison (UWA, WAIMR, other universities); supervision of the research group of neurogenetics; overall management of research activities. Planning and implementation of research into the genetic basis of psychiatric disorders. Research topics: identification and characterisation of candidate genes in schizophrenia; studies on the genetic basis of alcohol and substance dependence.
Collaborative Researchers (Clinical Research Centre, North Metropolitan Health Service Mental Health)

Johanna C Badcock PhD MA (Clinical), BA (Oxon.)
Specialist Clinical Psychologist

(08) 9347 6507
jo.badcock@health.wa.gov.au

Prof Badcock is a psychological scientist; her research focuses on how cognitive processes drive the symptoms of mental illness, such as auditory hallucinations. Her particular expertise lies in cognitive and neuropsychological assessment. Prof Badcock’s program of research also includes a systematic examination of attitudes to mental illness in the general community and in mental health professionals.

BAHRI, Lorraine
Administrative Assistant

(08) 9347 6429
lorraine.bahri@health.wa.gov.au

General administrative and secretarial support; Occupational Health and Safety representative.

BOSE, Avijit, BSc (Human Physiology), Diploma in Neurophysiology, Electroencephalography
Neurophysiology Technologist

(08) 9347 6593
avijit.bose@health.wa.gov.au

Assists with day-to-day technical and administrative work within the neurophysiology and related units. Prepares subjects for neurophysiology recordings and procedures. Conducts standard assessments. Conducts neurophysiology recordings. Conducts standard neurophysiological procedures (EEG, ERP, rTMS, TCSD). Establishes interactive parameters. Assists with preparation of reports and other publications. Participates in quality improvement and internal audit activities. Assisting in research and data collections.
DRAGOVIC, Milan, BPsych, PhD
Senior Scientist - Neuropsychiatry
Adjunct Associate Professor, School of Psychiatry and Clinical Neurosciences, UWA

(08) 9347 6442
milan.dragovic@health.wa.gov.au

Biostatistical support to CCRN research: complex multivariate analyses, structural equation modelling; latent class and fuzzy cluster modelling, genetic linkage and association analyses, managing major research databases.

MORAR, Bharti
Laboratory Research Officer

(08) 9346 4615
bharti.morar@health.wa.gov.au

Responsible for the processing and regular maintenance of biospecimens isolated from blood samples collected from WAFSS patients and controls that are crucial for genetic studies. Performs complex cell culture procedures on these samples and is involved in molecular studies undertaken as part of WAFSS research projects. She manages the genetics laboratory and databases related to the WAFSS biospecimen collection.
PRICE, Greg  
*Senior Scientist - Electrophysiology*

(08) 9346 6493  
greg.price@health.wa.gov.au

Dr Price has two decades of experience in electrophysiological research in mental health at Graylands Hospital in Perth. He manages the EEG/ERP components of CCRN as an affiliated researcher in the WAFSS project. Arising from his experience in conducting clinical EEG services, his research has focused on schizophrenia and depression. The neurophysiological approaches include EEG and event-related potentials (ERP). His expertise is mainly in P300 studies, MMN, antisaccade task and P50 protocols in schizophrenia, affective disorder, and normative groups. Analyses include neural networks, syntactic analysis, wavelet and independent component analysis, as well as the standard ERP averaging approaches.

STEFANIS, Nikos  
*Winthrop Professor*

(08) 9346 6439  
stefanis.nikos@health.wa.gov.au

Early intervention in psychosis treatment; epidemiology and genetics of schizophrenia; impact of environmental factors on the development of psychosis.

WATERS, Flavie, MSc, MPsych (Clinical Neuropsychology), PhD  
*Senior Research Fellow*

(08) 9347 6650  
flavie.waters@health.wa.gov.au

Dr Waters investigates the cognitive and neurobiological bases of neuropsychiatric disorders, with a focus on schizophrenia and other psychiatric conditions affecting older adults. Her research program uses a cognitive neuropsychiatric approach with clinical application components.
Centre for Clinical Research in Neuropsychiatry

Location/Courier Address
Gascoyne House
John XXIII Avenue
Mt Claremont, Western Australia 6010

Postal Address
Private Bag No 1
Claremont, Western Australia 6910

UWA Internal Mail
M708

Telephone
(+61) 08 9347 6429

Fax
(+61) 08 9384 5128

Email
lorraine.bahri@health.wa.gov.au

Website

Gascoyne House – Map Location: