Queensland Centre for Mental Health Research: the first 17 years

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Objective: To reflect on the establishment and evolution of the Queensland Centre for Mental Health Research.
Method: Narrative historical review.
Results: First established as an inpatient research unit in December 1987, the focus of the Centre evolved in concert with the skills of the staff. After the structure was revised in 1996 and 1999, the Centre has evolved into a group with four main research streams – epidemiology, developmental neurobiology, genetics and policy and economics. Although the group maintains a strong focus on serious mental disorders such as schizophrenia, our policy and economic work has a wider perspective. The Queensland Centre for Mental Health Research is based in an historic mental health service, with laboratories in collaborating universities and institutes. Key lessons learnt by the group along the way relate to the importance of focusing on a restricted range of research topics in order to build a critical mass.
Conclusions: Given a facilitating environment, hospital-based research groups can prosper. Over the last 17 years, a cost-efficient, focused and productive research group has evolved that has made contributions to international research.
Key words: epidemiology, genetics, policy, research, schizophrenia.

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Researchers develop skills at turning the harsh glare of the spotlight onto particular research topics, but tend to become rather shy when asked to make the research group itself the subject, rather than the object, of scrutiny. The invitation to review the development of the Queensland Centre for Mental Health Research (QCMHR) not only provides us with an opportunity to document our recent history, but also to reflect on critical factors that may have contributed to our current strengths. We sincerely hope that the reader finds this rather self-indulgent task both interesting and instructive. Just as we are grateful for the support of colleagues in our early days, we hope that others can profit from our experience. Of course we are much too close to the object of scrutiny to provide a balanced assessment – we will leave that for our peers and to future researchers. We also have to walk the tightrope of balancing great pride in our achievements with a suitable degree of modesty. This paper will outline the history and evolution of our group and provide a snapshot of our current research.

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Early days: a clinical research unit at the asylum

The idea of basing a research group at the Wolston Park Hospital near Brisbane was met with scepticism and disbelief by the psychiatric establishment in the late 1980s. Opening in 1865, the hospital had been through

the usual mutations in name and function, reflecting the changing needs of mentally ill people and had accumulated the usual stigma associated with these facilities. By the time our group was established, the hospital was looking decidedly neglected with all the action being in general hospitals and community services. External reviews often used the Wolston Park Hospital as an example of an under-resourced, outdated service and, on a national basis, the hospital ranked very poorly. Teaching hospitals in Brisbane tended to view the hospital as a 'bin' for difficult patients.

In 1984, Dr Harvey Whiteford was provided with a Queensland government scholarship to study overseas. He worked in the Clinical Research Unit of the Palo Alto Veterans Administration Medical Center (VAMC), a teaching hospital of Stanford University. As part of his negotiations to return to Queensland he secured a commitment that one ward at Wolston Park Hospital would be redeveloped, along with all its staff, into a research unit. The administration of the Health Department saw this, in part, as a way to attract staff to the facility and to encourage a more reflective and evidence-based clinical perspective. Against considerable odds (including resistance from nursing unions), a 26-bed inpatient unit was established in McDonnell House. The word 'research' was not permitted in the title and the unit was named the Clinical Studies Unit, a title borrowed from the unit where another Australian, Bernard Carroll, worked at the University of Michigan.

During these early days, research skills were limited. Harvey Whiteford used the Palo Alto VAMC model to structure the Unit and established, with Terry Stedman, an inpatient psychopharmacology research program. In collaboration with Professor Sue Pond, a small laboratory was established at the Princess Alexandra Hospital under the direction of Dr Darryl Eyles. As a result of necessity rather than design, laboratory staff were based in off-campus facilities, a model that was soon to be replicated for our other groups. The disadvantages of having staff spread out over several campuses were more than compensated by cost savings and by the intellectual and scientific cross-fertilization that can follow these decisions.

In 1987 the psychopharmacological treatment of schizophrenia was a rather stale and uninspiring domain. Research groups were (and still are) desperately looking for 'add-on' products that could potentiate the clinical efficacy of the traditional antipsychotic medications. In this vein, early projects at the Clinical Studies Unit involved add-on studies of proglumide [1], nifedipine [2] and famotidine [3]. With the financial support from groups such as Schizophrenia Fellowship and intellectual encouragement from colleagues such as David Copolov and staff at the Victorian Mental Health Research Institute (MHRI), our group became proficient at clinical trials. Tardive dyskinesia was a prominent issue at that time and the first National Health and Medical Research Council (NHMRC) grant was secured in 1989 to study a related topic, the Clinical and Neuroendocrine Correlates of Neuroleptic Withdrawal, part of the search for a supersensitivity psychosis. During the early 1990s, the atypical antipsychotic medications were entering phase III trials. The Clinical Studies Unit was involved in early trials of risperidone, remoxipride, clozapine, olanzapine, quetiapine and ziprasidone. The infrastructure and staffing was finely honed to support these studies and over the first 10 years our group served the equivalent of their 'research apprenticeship'.

Broadening the research themes and skills

Apart from becoming efficient at psychopharmacology, these early days were characterized by capacity-building and the addition of new staff and skills. John McGrath joined the group in 1988 and in 1990 took over the role of Director from Harvey Whiteford, who had been appointed Director of Mental Health in the Queensland Health Department. In 1992, at the invitation of Harvey, Bryan Mowry joined the group, having previously established a schizophrenia genetics research program in Perth.

The injection of new skills was translated into a broad, multidisciplinary research program, that we affectionately now label our 'promiscuous phase'. We were keen to do any type of research with anyone who would collaborate with us. Not all of this research effort resulted in quality outputs, but it did allow the team to expand our skill base and develop many new ideas. The recurrent funding from the Queensland Health Department served a critical role in incubating projects, not all of which were carried forward during subsequent restructuring.

In the 1990s the Cochrane Collaboration reminded clinicians about the need to make clinical decisions based on high-quality evidence. During that time Paul White, Robyn Hayes and John McGrath contributed to over a dozen Cochrane reviews [4–15]. The discipline of these studies was to imprint on our staff and our group was among the first to apply systematic review and meta-analytic techniques to descriptive epidemiology [16–18]. Other projects examined the needs of parents with serious mental illness [19–24], the identification of psychoses in Aboriginal and Torres Strait Islander populations as well as in correctional settings and in the measurement of quality of life in patients with mental illness [25–27].

Forging a more productive research group

Just as a sword needs to be forged by repeated heating and hammering, a research group must remain flexible and responsive. By the mid-1990s, our group was aware that we needed to restructure. Over two-thirds of our budget was required to staff the inpatient unit and an audit of skills showed that while we had many loyal and talented staff who could run drug protocols and score psychopathology, we had painfully few staff who could write grants and papers. Running trials for the pharmaceutical industry became increasingly less attractive to the staff. By this stage we were also building momentum in laboratory-based research. After a period of consultation and reflection, in 1996 we closed the inpatient unit and used the savings to fund more senior positions (including post-doctoral level scientists, research and business managers). Renamed as the Queensland Centre for Schizophrenia Research, we elected to focus on fewer topics and began to build teams around key areas in order to produce a critical mass.

Our unit was not the only part of the hospital undergoing change. As part of the 10-year Queensland Mental Health Plan, Wolston Park Hospital was to be rebuilt. A long and difficult period of change swept over the entire hospital, as slowly wards were closed and staff redeployed. Underpinning the change, an energetic district and hospital executive team (Mark Waters, Pam Lane, Kevin Fjeldsoe, Terry Stedman), began a change-process that was the most far-reaching in the 130-year history of the hospital. By 2002 a new 175-bed hospital was opened that provided state- and district-level services for secure patients, extended treatment and rehabilitation and dual disability. Within the mission and name of the facility, research and education were to figure prominently. Our research centre was moved to a refurbished building within the new hospital, now called The Park Centre for Mental Health Treatment, Research and Education. Of all the features underpinning our current success, one of the most important was the support and encouragement from the district and hospital executives. After a long journey we had a sense of loyalty and 'belonging' to the new hospital.

Hospital restructures are a good time to make changes, so we used the hospital-wide redevelopment to fine-tune our structure and research focus. Based on 'research on research', critical mass is often a key feature of productive teams. In 2000 Harvey Whiteford was returning to Brisbane from the World Bank. He was invited to join our team to establish a new group focusing on policy, economics and services research. Not only were we excited about attracting Harvey back to the unit, but we were keen to design a research portfolio that had more proximal outcomes for consumers and caregivers, as well as the more long-term and grandiose goal of finding the causes of schizophrenia.

In response to the changing landscape of clinical services, our group evolved into its present form, with four main research groups (Epidemiology, Developmental Neurobiology, Genetics, Policy and Economics) and a Research Operations group (including Dr Trish Nolan, Research Manager, Mr Mario Gryl, Business Manager, as well as administrative and IT support).

In 2003 we made changes to the management structure of our group to better reflect the depth of expertise that has been acquired over our history. Instead of appointing a permanent Director to head QCMHR, we have adopted a process similar to that used by universities for department heads. This responsibility was shared between the directors on a 3-year rotating basis. In contrast to many other research groups, QCMHR operates as a business unit within a hospital and a health district. We report to the hospital executive, rather than to a board of directors or to an advisory board. Also, in contrast to groups such as The Neuroscience Institute of Schizophrenia and Allied Disorders (NISAD), we have focused all our efforts on the core business of research, rather than public education or fundraising.

The next section will outline in more detail the achievements of the four research groups.

Epidemiology

Influenced by the discoveries in the late 1980s linking prenatal influenza epidemics and risk of schizophrenia, epidemiology became a research focus. The Queensland Mental Health Statistics System had person-linked data on all inpatient psychiatric admissions in the state. John McGrath and Joy Welham explored season of birth [28,18,29] and the influence of influenza epidemics on schizophrenia birth rates [30]. Age at first registration was also relatively readily accessible in this dataset [31,32]. In collaboration with Assen Jablensky (Centre for Clinical Research in Neuropsychiatry, CCRN) and other coinvestigators in Melbourne and the Australian Capital Territory, our group assisted in the landmark National Survey of Psychotic (low prevalence) Disorders [33,34]. The epidemiological framework allowed us to add on a risk-factor study, which has provided data on a range of factors including paternal age [35], urban birth and migrant status [36], minor physical anomalies [37] and dermatoglyphic patterns [38].

Based on the season of birth effect, and other curious features of schizophrenia epidemiology (an increased risk in urban-born, an increased risk in black migrants

living in cold countries), in 1999 we proposed that low prenatal vitamin D may be a risk-modifying factor for schizophrenia [39,40]. Parallel with our animal experiments, our group has been collaborating with international researchers on epidemiological research related to the vitamin D hypothesis. If seasonal fluctuations in maternal vitamin D levels underlie the season of birth effect, then one would predict that the amplitude of this effect would be larger at higher latitudes (where ultraviolet radiation is weaker for longer periods of the year). Recently, we published a systematic review and meta-analysis of season of birth studies from the northern hemisphere [16]. A small but significant association between the size of the winter/spring excess and latitude was found ($r = 0.271$, $p < 0.005$).

Besides ecological research, we have examined the hypothesis using more analytical epidemiological designs. We directly measured maternal 25-hydroxyvitamin D_3 levels in blood sera taken during the third trimester and banked for four decades, in collaboration with colleagues from the Harvard School of Public Health (Steve Buka) and Johns Hopkins University (Bob Yolken). The study suggested that vitamin D levels below a critical threshold may be associated with an increased risk of schizophrenia [41]. In a study with colleagues from the University of Oulo (Matti Isohanni) and the University of Cambridge (Peter Jones), we found a link between the use of vitamin D supplementation during the first year of life and a reduced risk of schizophrenia in males only (based on the Northern Finnish Birth Cohort) [42].

In 2004 our group published a major review of the incidence of schizophrenia [17]. After 3 years of back-breaking work, our team identified 100 traditional (or core) studies, 24 studies reporting the incidence in migrant versus native-born, 23 studies reporting the incidence of schizophrenia based on cohort and 14 studies based on subgroups of the population (e.g. twins, the deaf etc.). These studies, which were drawn from 33 countries, generated a total of 1458 rates. Based on discrete core data for people (55 studies and 170 rates), the distribution of rates was asymmetric and had a median value (10–90% quantile) of 15.2 (7.7–43.0) per 100 000 people. The distribution of rates was significantly higher in males compared to females; the male/female rate ratio median was 1.40. Those studies conducted in urban versus mixed urban–rural catchment areas generated significantly higher rate distributions. The distribution of rates in migrants was significantly higher compared to the native-born; the migrant/native-born rate ratio median was 4.6. This study showed that there is a wealth of data available on the incidence of schizophrenia. The width and skew of the rate distribution, and the significant impact of sex, urbanicity and migrant status on these distributions, indicate substantial variations in the incidence of schizophrenia. We will shortly complete a companion study related to the prevalence of schizophrenia. Apart from developing new methods to synthesize these studies, we have lodged the entire dataset with the publication (in a full, free-text electronic journal) in order to make the data available for data mining.

Developmental neurobiology

The neurodevelopmental hypothesis of schizophrenia proposes that genetic and epigenetic factors alter early brain development, leaving the affected individual at increased risk of developing schizophrenia [43,44]. However, the relative inaccessibility of the fetal brain, combined with the long lag between the putative early life insult and the onset of psychiatric symptoms, have hindered research into the neurodevelopmental hypothesis. These difficulties are exacerbated by the lack of ready *in vitro* tissue culture models from the adult brain that could be used as surrogates for early brain development. The ability to establish cell cultures from human brain tissue is restricted because: (i) the vast majority of neurons are terminally differentiated and thus have lost the ability to differentiate in culture; and (ii) any procedure to harvest neurons from the human central nervous system (CNS) is fraught with risk and technical difficulties. In collaboration with Professor Alan Mackay-Sim, QCMHR has forged a close and productive alliance with the School of Biomedical and Biomolecular Science at the Nathan campus of Griffith University. We published the first study of olfactory neuroepithelium in schizophrenia versus controls and discovered informative group differences that have led to several new lines of research [45,46].

Dr Francois Feron, one of our staff, was able to isolate ensheathing cells from this tissue, which opened up new horizons for neuroscience. These cells had been shown to facilitate healing of spinal cord trauma in animals. In collaboration with a large team of researchers, a clinical trial of these cells in spinal repair is currently underway in Brisbane. These discoveries were a 'spin off' from our schizophrenia research and have attracted international attention. Currently, we are looking at adult stem cells isolated from the olfactory biopsy tissue and using high-throughput genomic methods to explore schizophrenia and bipolar disorder.

Inspired by the hypothesis that low prenatal vitamin D may alter brain development, our group co-ordinated a major research program based at both Griffith University and the University of Queensland. Under the direction of Dr Darryl Eyles, our group has now proven that low prenatal vitamin D impacts on brain development in the rat. We have shown that maternal

depletion of vitamin D leads to rat pups with longer brains and larger lateral ventricles, with increased cell proliferation and reduced apoptosis, and reduced neurotrophin receptor (p75) and reduced levels of the nerve growth factor (NGF) and glial cell line-derived growth factor [47]. This and related studies [48,49], showed that low prenatal vitamin D is a biologically plausible candidate risk factor for neuropsychiatric disorder. In 2002 we were joined by Dr Tom Burne, a behavioural neuroscientist. Recently, we have explored the subtle behavioural changes associated with this animal model [50,51].

Genetics research program

There is good evidence from family studies that genes play an important causative role in this disease, and twin and adoption studies confirm this, but the pattern of inheritance is complex [52]. Available data suggest multiple genes, each exerting small-to-moderate effect on overall disease risk, interacting with environmental factors in a neurodevelopmental context to confer vulnerability [53]. The exact number and population frequencies of these susceptibility genes are still unknown.

The molecular genetic revolution has enabled the search for disease genes. Before the mid-1970s, the only markers available for mapping diseases were blood groups, serum proteins and HLA tissue types relating to only a handful of chromosomal locations. With the discovery of certain enzymes' ability to cut DNA by recognizing specific sequences of 4–6 base pairs in length, restriction fragment length polymorphisms (RFLPs) were created for use as genome-wide markers for mapping disease genes. Polymerase chain reaction (PCR) method made it possible to amplify genome-wide, highly polymorphic microsatellite markers (short tandem-repeat polymorphisms or STRPs), superseding RFLPs. Single nucleotide polymorphisms (SNPs) involving a single base change are now also being used because they are easily detected, adaptable to high throughput, automated typing and they are abundant, occurring one in every 1000 base pairs, based on results of the Human Genome Project and Celera Genomics. This is an important time for psychiatric genetics generally, and for schizophrenia in particular. Considerable progress has been made in the last few years towards identifying susceptibility genes. Although many candidate genetic loci have not been replicated, a modest number of chromosomal regions have emerged that continue to look promising. Recently, there have been a number of biologically plausible candidate genes attracting support from independent studies, including microarray studies.

Our program contributes to the above literature and has expanded over the last decade with continuous funding primarily from the NHMRC and the National Institute of Mental Health (NIMH). We have focused on the recruitment and diagnostic ascertainment of family samples from both ethnically diverse and ethnically distinct populations in Australia, Fiji, Sarawak and India. In addition, we have studied the phenotype/genotype relationship in these cohorts. Because schizophrenia is clinically heterogeneous, it is important to rigorously define this phenotype [54] and to investigate whether genetically distinct subtypes exist [55]. These investigations depend on the availability of detailed clinical data and on correlated endophenotype data such as MRI imaging, neuropsychological profiling and neurophysiological testing.

Independent and collaborative molecular genetic analyses

Some details of our studies will now be presented.

In collaboration with Douglas Levinson (University of Pennsylvania, Philadelphia) we conducted a genome scan on 43 pedigrees (18 Australian, 25 US), using a map of over 300 genetic markers. At the time, it was the third and largest published schizophrenia scan, with regions on chromosomes 2q, 4q, 9q, 10q and 11q providing nominal evidence for genetic susceptibility [56]. Subsequent fine-mapping analysis of these regional findings, conducted at the Australian Genome Research Facility, provided support for the initial findings on chromosomes 2 and 10 [57]. These data recently contributed to an influential meta-analysis of schizophrenia genome scans [58], which identified a greater consistency and convergence of linkage results across studies than previously recognized, with consequent support for a relatively small number of loci being implicated in schizophrenia susceptibility. In addition, our group has continued to contribute to methodological issues [59,60,45] and to the analysis of the field's most prominent hot-spot regions both separately [62–64], and as part of multi-site collaborative analyses, including the investigation of defined chromosomal regions on 22q [65], 3p, 6p and 8p [66], Xp [67], on 5q, 6q, 10p and 13q [52] and more recently on 1q [68] and 22q [69]. To follow up the original 6q linkage finding by Pablo Gejman (Northwestern University, Chicago), we are collaborating with his group on linkage [70] and candidate gene studies [71–73] in this region. In addition, we are collaborating with US groups to conduct molecular genetic studies on a large affected sibpair cohort (recruitment finalized) and a large case–control cohort (recruitment underway). It is important to note that the complexity of the clinical and genetic data makes the recruitment and

standardized assessment of large (collaborative) samples imperative.

There are also a number of studies of ethnically distinct populations underway. First, in collaboration with Jude Ohaeri, St Giles Hospital, Suva, a sample of indigenous Fijian and Indian Fijian subjects with psychotic disorders have been recruited for gene mapping studies using linkage disequilibrium analysis [62]. Second, in collaboration with Robert Barrett, University of Adelaide and with the University of Malaysia, Sarawak, we are conducting a clinical and genetic study of schizophrenia in the Iban, an indigenous people of Malaysia [74]. Finally, a schizophrenia study in Tamil Nadu is underway in collaboration with Rangaswamy Thara and her team at the Schizophrenia Research Foundation, Chennai, India.

To complement pedigree studies in the search for potential causative factors for psychosis, both genetic and non-genetic, we, in collaboration with state and national colleagues, have been funded to conduct a study of Australian twins with psychosis, involving a series of clinical, neurobiological and genetic investigations.

To date, finding candidate genes for schizophrenia has proven elusive but the stage is now set for accelerated progress towards discovery. Identifying causative mutations within these genes will help us to understand the pathophysiology of this disease, to develop more effective, specific therapies and to provide a clearer perspective on the role of non-genetic factors as targets for preventive strategies.

Policy and economics

Our historical emphases on aetiology and clinical treatments for schizophrenia expanded with the establishment of the Policy and Economics Group in 2001. The research of this group is in three areas – the process of mental health policy formulation, the implementation of policy (specifically how interventions and services are organized, financed and delivered) and the outcomes achieved through policy and service reform (especially in terms of equity and efficiency). Just as the other QCMHR programs of research have forged strong ties with basic sciences, the Policy and Economics Group has developed close links with areas such as population health, social policy, economics, politics and government [75].

For this type of research to be relevant it is important to work directly with policy makers and stakeholders within and outside government and we are fortunate to have been able to work closely with national governments and international agencies in both established market economies and developing countries. In the area of policy development this has lead to our close involvement in the drafting of the Australian National Mental Health Plan 2003–2008, in leading the International Consortium on Mental Health Policy and Services [76] (http:www.world-mental-health.net) and in consulting to the WHO Mental Health Policy Project (http://www.who.int/mental_health/policy/en) and the South East Europe Mental Health Project.

For us, research in policy development must be complemented by an understanding of how it is implemented and the outcomes achieved during the implementation. In this we have been keen to learn from what has happened in the past and have evaluated a number of policy initiatives adopted under Australia's National Mental Health Strategy [77]. Our capacity in economic analysis was enhanced when Darrel Doessel joined our group from the School of Economics at the University of Queensland in 2002. Dr Doessel is undertaking research to describe and explain the various financial outcomes, in terms of net and gross prices for consumers and subsidies for psychiatric services, payable by the Commonwealth Government. He has also evaluated the efficacy of a Commonwealth Government policy which changed the rebates offered to people using a large number of psychiatric services (Item 319) and examined the economic consequences of de-institutionalization before and after implementation of the National Mental Health Strategy in 1993 [78].

We further strengthened our services research capacity when we were joined by Philip Burgess who took up the first Chair in Mental Health Services Research at the University of Queensland in 2003. Dr Burgess brought with him specific skills in assessment of mental health needs [79] and outcome analysis; the latter leading to his being awarded the contract, along with Jane Pirkis from the University of Melbourne, for the analysis, reporting, mental health outcomes and casemix development component of the Australian Mental Health Outcomes and Classification Network (http://www.mhnocc.org/). Our interests in government policy, service reform and cost effectiveness of mental health interventions in developing countries led to our involvement in projects with the World Bank and World Health Organisation, such as the Disease Control Priorities in Developing Countries Project (http://www.fic.nih.gov/dcpp)

A recent focus has been on work and mental health. This has taken two forms. The first involves research to measure and improve long-term vocational outcomes in people with mental disorder, with a focus on labour market participation and predictors of employment outcomes of people with both psychotic disorders and higher prevalence disorders [80–82]. The second area focuses on high prevalence disorders in people who are in remunerated employment. The key project in this area is the identification of costs and productivity benefits, including in dollar

terms, of screening and treating depression in the Australian workforce (http://www.worc.qcmhr.uq.edu.au).

Conclusions

Our group has evolved in response to the changing face of psychiatric research and also as a reflection of the skills of the senior investigators. We have evolved against a background of modernization of mental health services in our state. We have also directly and indirectly benefited from Queensland Smart State initiatives. One of our senior collaborators (Professor Alan Mackay-Sim) was made Queenslander of the Year in 2003–2004. One of our staff, Francois Feron (recently appointed to a Chair at the University of Aix-Marseille, France), was given an Excellence Award from the Director General of Health for his discoveries related to the isolation of ensheathing cells from nasal biopsy. John McGrath was awarded the Premier's Award for Biomedical Science (an award auspiced by the Australian Society for Medical Research) in 2003 and a Queensland–Smithsonian Fellowship to pursue his collaboration with colleagues at Harvard University. We are benefiting from Smart State infrastructure grants awarded to the University of Queensland (the new Queensland Brain Institute) and Griffith University (Eskitis Institute for Cellular and Molecular Therapies) and from Commonwealth funding to the Queensland Institute of Medical Research for a proteomics facility. Queensland Institute of Medical Research's high-throughput genotyping platform continues to be a vital platform for our genetics studies.

Over the years we have enjoyed collaborations with many interstate (NISAD, MHRI, CCRN) and international collaborators. These have been productive from a research perspective and also personally rewarding. Consumers and caregivers have been a great source of inspiration to our group. Being based on a long-stay hospital is a constant reminder of the unmet needs of people with serious mental illness. Not only have these consumers contributed to our research as participants, but as friends and coinvestigators. As can be seen in the gallery on our website (www.qcmhr.uq.edu.au), many are highly talented artists.

In September we celebrated our name change, new premises and the addition of Harvey Whiteford's group with a formal opening ceremony by the Minister for Health, the Honorable Gordon Nuttall. To some it may seem strange that a group operating since 1987 has a formal opening in 2004. To explain, our 'opening ceremony' was not so much a beginning as a 'coming of age'. We feel we have completed an important developmental phase and have begun a new era of focused, productive and efficient research.

As a group, we have learnt many lessons about how best to do mental health research. For example, we have learnt how important it is for a research group to change and to have the courage to concentrate skills in the most productive areas. We have delivered efficiencies by concentrating on a limited range of topics and providing each stream with the critical mass to achieve their research outcomes. We have fashioned a research portfolio that provides both proximal and long-term outcomes. We look forward to continuing to contribute to the global research efforts to reduce the burden of mental illness. A significant part of this burden can be reduced by better mental health policy and services, but an even greater proportion of the burden is unavertable with our current treatments. As researchers, we need to have a sense of urgency about the task at hand and keep focused on ways to reduce this burden.

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