SCHIZOPHRENIA RESEARCH INSTITUTE

McKeon Review Secretariat
PO Box 4226
MANUKA ACT 2603

23 March 2012

Re: Submission to the Strategic Review of Health and Medical Research in Australia

Dear Panel Members

Please find attached a submission for your consideration, which is of particular relevance to item 8 in the terms of reference: *Opportunities to improve national and international collaboration between education, research, clinical and other public health related sectors to support the rapid translation of research outcomes into improved health policies and practices*.

This proposal outlines how clinical service provision and patient outcomes in severe mental illness could be significantly improved by developing a pragmatic clinical trials network, thereby embedding research activities into routine clinical practice.

There is a paucity of reliable information on how existing pharmaceutical and psychosocial treatments could best be targeted to people with severe psychotic illnesses. Without appropriate guidelines, clinicians are left to rely on personal experience when deciding how to treat severe and complex mental illnesses such as schizophrenia, bipolar disorder, and related psychotic illnesses, which consequently remain costly and burdensome for Australia's health system.

There are significant improvements in the efficiency and effectiveness of Australia's health system to be gained through the integration of research activities into clinical practice. A psychosis clinical trials network would confer the following benefits:

- Better patient outcomes through targeted treatment combinations and guideline development, particularly for treatment-resistant illness.
- Generation of information on treatment safety and adverse effects in a real-world setting.
- Dissemination and ongoing evaluation of newly-developed treatments through the existing trials infrastructure.
- A culture of support for research by mental health clinicians and a platform to enable research training will be developed.
- A sound evidence base to support policy makers and improved uptake of evidence-based treatment approaches by Australia's mental health workforce.

Translation of research outcomes into health policy and practice requires an integration of research activities into clinical practice settings. A pragmatic clinical trials network would confer significant benefits for mental health care in Australia, through research translation and the continual improvement of clinical services.

If you would like more information on any aspect of this submission, I can be contacted on v.carr@unsw.edu.au or (02) 8382 1410.

Yours sincerely,

Vaughan Carr

CEO & Scientific Director

TRANSLATIONAL RESEARCH IN MENTAL HEALTH
How research can improve quality of clinical care in mental health – and inform mental health policy

The shift towards evidence-based practice has not sufficiently permeated public mental health services. There is an efficacy-effectiveness gap. First, many treatments of known efficacy in specialized research settings, as demonstrated in randomized controlled trials, are *not* widely implemented in routine clinical practice. This is particularly the case for psychosocial treatments (eg, family interventions, cognitive-behaviour therapy, supported employment programs). Second, many treatments of known efficacy in specialized research settings that *are* implemented widely (especially medications) are of uncertain effectiveness in routine clinical practice.

It has long been acknowledged that evidence-based practice requires that research be seen as integral rather than separate from clinical practice,[1] but this has not generally occurred in Australian public mental health services. Consequently, mental health services are characterized by high levels of uncertainty in decision making, both at the level of individual patient care and at the policy level. Improving the quality of mental health care requires that such uncertainty be reduced. This can be achieved by greater support for evidence-based practices in the form of comparative effectiveness research.[2]

Comparative effectiveness research (CER) compares the benefits and harms of different interventions and strategies to prevent, diagnose, treat and monitor health conditions in *'real world'* settings. CER comprises pragmatic or practical clinical trials, retrospective studies using administrative datasets, systematic reviews and other methods.[2] The Schizophrenia Research Institute already analyses, reports on and conducts systematic reviews in relation to schizophrenia, and these are publicly available.[3] A similar resource could be of use for other severe mental disorders as well.

Clinical trials are either *explanatory* or *pragmatic*. Explanatory trials address the question: "does treatment X work under ideal conditions?" Participants are required to meet very narrow selection criteria, study design is geared to demonstrate efficacy by maximizing differences between the active treatment and placebo or comparator, and the investigators seek to understand the mechanisms by which the treatment is associated with benefits or harms.[2] Such research is generally conducted in highly specialized settings with well trained research staff administering multiple clinical measurements on multiple occasions.

Conversely, pragmatic clinical trials (PCTs) address the question: "does treatment X work in ordinary clinical settings?" As such, PCTs are designed to measure 'real world' effectiveness and answer questions faced by decision makers at the clinical coal-face, in public policy and amongst third-party payers. PCTs attempt to answer simple, clinically relevant questions about treatments of known efficacy. All willing patients with the condition of interest may participate; there are no restrictive inclusion criteria. Treatment occurs in a wide

variety of ordinary clinical settings and is administered with flexibility, giving clinicians leeway to exercise their judgment as they would in practice. Comparison treatments are either 'usual practice' or best available alternatives. Clinical ratings and protocol adherence measures are unobtrusive with minimum burden to patients and clinical staff. Follow-up is of low intensity and administrative databases are preferred for detecting outcomes, which must be objectively measured and clinically meaningful. A detailed description of PCTs in comparison to explanatory trials has been given elsewhere.[4]

Examples of influential PCTs conducted overseas include the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE)[5] and Sequenced Treatment Alternatives to Relieve Depression (STAR*D)[6] in the USA, and the Bipolar Affective disorder: Lithium/Anti-Convulsant Evaluation (BALANCE),[7] an international collaboration. Each of these PCTs provided invaluable information for helping to improve clinical practice and to guide policy development.

The following are some of the direct and indirect benefits of PCTs.

1. Improved patient outcomes. (a) Participants in a successful PCT will have better outcomes, including those assigned to the less effective treatment when they are switched to the more effective treatment at the completion of the PCT. (b) Future patients will have better outcomes when practice changes as a result of successful PCTs. Over time, an accumulation of knowledge about treatment effectiveness will lead to incremental improvements in outcomes as new benchmarks for quality of treatment are progressively established and superseded.
2. Important safety information will be generated from the large number of participants in PCTs in which the prevalence and relative risks of adverse events (including rare events) can be estimated more accurately than in current post-marketing surveillance of prescribed drugs.
3. The dissemination of new treatments of known efficacy, as demonstrated in explanatory trials (including psychosocial treatments), will be facilitated through PCTs that introduce these new treatments to clinical practice.[8] Clinicians who participate in PCTs are more likely to practice according to the results of such trials.
4. Policy makers will have a sound evidence base upon which to make decisions about service delivery and resource allocation.
5. Less tangible benefits include: (a) fostering a culture of measurement that has clinical relevance and immediate utility in clinical settings (as opposed to administrative reporting requirements); (b) encouraging a culture of critical appraisal of evidence and evidence-based decision making in clinical settings; (c) enrichment of the working environment that will help to attract and retain high quality clinicians; and (d) enrichment of the therapeutic environment in which patients and their families can sense that they are receiving best practice care and treatment.

Establishing PCTs to achieve the above benefits requires the following infrastructure.

1. Networks of clinicians, clinical academics and administrators working in partnership need to be established. These will have to be supported by a coordinating centre or centres with access to research expertise (clinical trial experts), biostatistics expertise, administrative support and adequate IT systems for data management and analysis. Such infrastructure will need to engage in recruiting to the broad network individuals and clinical sites representative of the mainstream of services and institute a combination of financial, practical and altruistic incentives to make participation in the network reasonable and attractive.[4]
2. Develop training programs in clinical measurement – for research *and* clinical decision-making purposes – as well as training in the design and conduct of PCTs for site investigators and their supporting clinical teams.
3. Develop PCT protocols that match best clinical practice, address significant clinical problems and/or gaps in the evidence, and that are short, user-friendly, evidence-based and clinically meaningful.[4]
4. Establish a governance structure for the network(s) described above, including consumer/carer input at several levels.
5. Provide adequate resources to support the PCT network for a period of 5 years and then evaluate its costs/benefits to determine whether and at what level recurrent funding is justified.

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