



Alberta Addiction & Mental Health  
Research Partnership Program

Alberta Centennial Mental  
Health Research Chairs  
Program



**Dr. Jean Addington – Annual Report**

website version

# Dr. Jean Addington

Alberta Centennial Mental Health Research Chair  
Inaugural Chair in Child and/or Adolescent Mental Health

## EXECUTIVE SUMMARY

Psychotic disorders, including schizophrenia and affective psychotic disorders are common, affecting about 5% of the general population. Development of these disorders usually results in significant disability, and psychotic disorders rank among the top 10 causes of disability worldwide. Psychosis is “brewing” long before its manifestation as a diagnosable illness and there are identifiable signs and symptoms that precede the development of frank psychotic symptoms. Over the last decade there has been a worldwide movement to develop comprehensive early intervention programs for schizophrenia. However there is now compelling evidence that in the pre-psychotic phase the formation of symptoms, and disability changes have already begun. My work focuses on early detection of psychosis at both the pre-psychotic i.e. period of clinical high risk and at the first episode.

A major focus of my work is participating in the NAPLS consortium. NAPLS represents a collaboration of eight clinical research centers based at Emory, Harvard, North Carolina, UCLA, UCSD, Yale, Zucker Hillside Hospital and myself first in Toronto and now in Calgary. In a prior phase of our consortium, NAPLS 1, we pooled clinical and psychosocial data obtained on a large sample of patients (N=291) who had been ascertained using a standardized set of operational diagnostic criteria for a “prodromal” risk syndrome. Risk for onset of psychosis in this population was 35% after 2 and 1/2 years of follow-up, with a decelerating rate of conversion over this period. Moreover, prediction algorithms incorporating baseline clinical and psychosocial variables dramatically improved positive predictive power (~80%) compared with the prodromal criteria alone, but achieved only modest sensitivity (~40%). Our goal is in NAPLS 2 which runs until 2013, to improve upon these prediction algorithms by incorporating biological measures with clinical measures and to test the possible differential course of change in biological indicators in those who convert to psychosis.

The potential utility of biological assays in elucidating predictors and mechanisms of psychosis in the prodromal population is thus far based exclusively on analyses of data collected at individual sites with small samples. For example, the UCLA team, working collaboratively with investigators in a prodromal program based in Melbourne, Australia, has recently demonstrated a significantly steeper rate of gray matter reduction in prefrontal cortical regions in prodromal patients who convert to psychosis compared with those who do not over a 1-year follow-up period. This pattern of accelerated change in prefrontal regions is mirrored in a sample of first-episode schizophrenia patients compared with age- and gender-matched healthy controls over a 2-year follow-up period. Together, these data suggest that during the prodromal and early phases of schizophrenia, there is an exaggeration of the regressive neuromaturational processes (programmed cell death, synaptic pruning) normative to late adolescence and early adulthood, changes that may participate

in the pathophysiology of psychosis onset. To test this model rigorously, while at the same time accounting for the marked heterogeneity in outcomes among prodromal and early psychosis patients, will require sample sizes many times larger than those available in any single site. In addition, ideally, any investigation into the course of gray matter reduction in the prodromal phase of psychosis would incorporate information from other assessment modalities (genomics, proteomics) that can reveal molecular mechanisms for the steeper rate of change in the converting group.

These putatively prodromal or clinical high risk young people are help-seeking individuals who require help for their presenting concerns as well as interventions to delay or prevent the onset of the psychotic illness. Medication trials have suggested positive outcome in terms of reducing current symptoms and possibly delaying onset. Concerns with side effects of medication and the limited number who are willing to try this treatment make a psychological intervention appealing; the potential value of psychological interventions is only supported by preliminary evidence. Thus, the potential third phase in this work would be to begin to test effective treatments to prevent and/or delay the onset of a psychotic illness. These treatments would be based on the outcome of the ongoing NAPLS project and from pilot work testing current available treatments. Thus, we are now moving to preliminary pilot work in treatment in anticipation of the third phase of this illness. We have begun to develop pilot projects of various treatments that we will be testing over the next two years. However, a comprehensive approach to early intervention requires not only the development of an effective treatment but also establishing that it is being offered to those who need it. This necessitates understanding more fully two relatively neglected areas: the pathways to care and the target population. These are areas in which we will also be developing projects over the coming year.

The overall objectives of my research are:

1. to determine the predictors of psychosis
2. understand the mechanisms of conversion to psychosis
3. determine means to identify young people in the earliest stages of psychosis
4. develop effective treatments for the earliest stages of psychosis

## **DEVELOPMENT OF RESEARCH PROGRAM**

During this second year we have continued to expand and develop an active research program. We were originally housed in the Heritage Medical Research Building but over the period of January - March we were preparing for our move to the 1st and 4th floors of the TRW Building in the Medical School. Our move was completed in May 2010. We are now part of the newly established Mental Health Research and Education Centre. In this new centre we have adequate space for the first time for all the research staff, post doctoral fellows and students. We have specific lab space for neurocognitive testing and electrophysiology assessments. Since my research program has to exist in conjunction with a clinical service, we continue with our efforts with the PRIME Clinic which is a specialized clinic for individuals at risk for psychosis that operates under the Early Psychosis Treatment Service at Foothills Hospital. We continue to be responsible for maintaining recruitment efforts (fliers, posters for the clinic); screening all potential referrals to the clinic and arranging clinic appointments.

We continue to actively recruit for post doctoral fellows and graduate students.

The research staff is funded from the both the Chair and from other ongoing funded projects. Currently we have 9 full time staff and one part-time person

## **OVERVIEW OF ONGOING RESEARCH**

**NAPLS 2** is an ongoing 8 site 2 year project called “Predictors and Mechanisms of Conversion to Psychosis” which was funded in September 2008 for 5 years by the National Institute of Mental Health (NIMH). Although this is an 8 site study where each site conducts an identical study, each site is independently funded. This study will have 720 clinical high risk for psychosis subjects (CHR) and 240 controls with 90 CHR subjects and 30 controls coming from Calgary. In terms of psychosis prediction, we seek to determine whether biological abnormalities preceding psychosis onset contribute to prediction of psychosis independently from that of the best performing clinical algorithms and whether they can be combined with the clinical measures to enhance predictive utility. Clinical areas include psychopathology, neuropsychology, social functioning and social cognition. Biological areas include imaging, electrophysiology, genetics and cortisol. All sites follow identical protocols but each site is the lead in terms of designing and supervising one of the areas under study. Calgary is responsible for the psychopathology, risk factors and social cognition and for the data management. This study began in October 2008 and will end in September 2013. As of June 30<sup>th</sup> the study is completely set up and recruitment is underway. We have recruited 43 clinical high risk subjects and 30 normal controls and are right on target with recruitment. Our education campaign is ongoing.

**RAISE** is a contract study that was funded by NIMH in September 2009. Funding was awarded to Dr. John Kane of Zucker Hillside Hospital with Dr. Jean Addington as one of the lead co-investigators. The purpose of this study is to develop a comprehensive treatment for first episode patients that includes both pharmacology and psychosocial interventions. This treatment will be such that it can be delivered in regular mental health centres in the USA as opposed to specialized first episode programs by regular mental health staff with minimal training and supervision.

**PREDICT** is a recently completed 3 site (Toronto, University of North Carolina, Yale) NIMH 5 year funded study of 260 putatively prodromal individuals and 100 help seeking controls examining predictors of conversion to psychosis.

**ADAPT** is a recently completed small RCT of CBT versus supportive therapy. The data has been analyzed and we have submitted several papers for publication.

**PSTEP** is a small RCT of CBT versus befriending that has now been completed. Data is ready for analysis.

**Preventing Morbidity Study** is an NIMH funded study with Dr J Kane of Hillside Hospital as the PI. This is an investigator driven study of metabolic side effects comparing the effectiveness of risperidone vs aripiprazole. Rater training for this study will be starting in the fall 2010 with recruitment to begin soon after.

## **KNOWLEDGE TRANSFER ACTIVITIES**

Knowledge transfer activities within Alberta have continued to focus on education about early detection in the pre-psychotic period.

### **EDUCATION FOCUS**

The purpose is to educate health care providers and families that there are research clinics and experimental treatments underway for those young people who are at risk of developing psychosis. The education effort began on February 2 2009 with a mass mail out of PRIME clinic information to all possible referral sources in Calgary. The goal was to increase awareness of the PRIME clinic and the Clinical High Risk state. During the spring and summer of 2009 a new PRIME website was developed with an emphasis on providing educational content that was suitable for youth, family and health care providers. At this time other educational materials were created including a Clinical High Risk symptom assessment chart, case studies and a NAPLS brochure to be distributed at presentations for mental health professionals. A NAPLS brochure for a general audience recently been completed, as has an information handout for new PRIME clinic clients.

The schedule for presentations was divided into three phases. The initial phase commencing September 2009 primarily targeted counseling staff at the secondary and post secondary level. Other essential referring sources that had contact with the 12 to 30 age group were also educated about PRIME and NAPLS. The next two phases of presentations — education of family physicians and the general public — will commence in fall of 2010.

#### **Presentations Given**

- Alberta Mental Health Board Telemedicine (2 presentations)
- ACCESS Mental Health (Alberta Health Services)
- University of Calgary Health Services
- Mobile Mental Health Response Team (Alberta Health Services)
- Schizophrenia Society
- Alberta College of Art and Design Counselling Services
- Boys and Girls Clubs of Calgary
- Mount Royal University Counselling Services
- Calgary Board of Education and Calgary Catholic School Board counsellors (4 presentations)
- ALEX Community Health Centre
- Wood's Homes Counselling Service
- NW Mental Health Clinic
- Catholic Family Services Counselling Service

SAIT Counselling Services  
Alberta Health Services Mental Health Resource Fair  
SAIT Disability Counselling Services  
Shared Mental Health Care (Alberta Health Services)  
Psychiatric Emergency clinicians (2 presentations)  
Mental Health Transitional Youth Services (Alberta Health Services)  
Village Square Community Health Centre (school based public health nurses)  
Parent Support Association (3 presentations)

### **Upcoming Presentations**

ACCESS Mental Health  
Mental Health Community Extension Team (Alberta Health Services)  
South Calgary Health Centre (all mental health staff)  
EXIT Community Outreach  
Child and Adolescent Mental Health Urgent Services (Alberta Health Services)  
Alberta Association of Family School Liaison Social Workers 21010 Conference

## **PUBLICATIONS**

### **(JULY 2009 –JUNE 2010)**

1. **Addington, J.**, & Tran, L., (2009). Using the Brief Core Schema Scales with Individuals at Clinical High Risk of Psychosis, *Behavioral and Cognitive Therapy*, 37, 227-231.
2. Woods, S.W., **Addington, J.**, Cadenhead, K., Cannon, T.D., Cornblatt, C., Heinssen, R., Perkins, D.O., Seidman, L.J., Tsuang, M., Walker, E., & McGlashan, T.H., (2009). Prodromal risk syndrome for first psychosis, *Schizophrenia Bulletin*, 35, 894-908.
3. **Addington, J.**, & Mancuso, E., (2009). Cognitive-behavioral therapy for individuals at high risk of developing psychosis. *Journal of Clinical Psychology*, 65, 879-890.
4. Walker, E., Cornblatt, C., **Addington, J.**, Cadenhead, K., Cannon, T.D., McGlashan, T.H., Perkins, D.O., Seidman, L.J., Tsuang, M., Woods, S.W., & Heinssen, R. (2009) The relation of antipsychotic and antidepressant medication with baseline symptoms and symptom progression: A naturalistic study of the North American Prodrome Longitudinal Sample. *Schizophrenia Research*.115, 50-57
5. **Addington, J.**, & Addington, D. (2009). Three year outcome of treatment in an early psychosis program, *Can Psychiatry*, 54, 626-30.
6. McGorry, P., Johanessen, J.O., Lewis, S., Birchwood, M., Malla, A. Nordentoft, M., **Addington, J.**, & Yung, A. (2010). Early intervention in psychosis: keeping faith with evidence based health care. *Psychological Medicine*, 40, 399-404.

7. **Addington, J.**, Girard, T.A., Christensen, B.K., & Addington, D. (2010) Social cognition mediates illness related and cognitive influences on social functioning in schizophrenia-spectrum disorders. *Journal of Psychiatry and Neuroscience*, 35, 49-54
8. Seidman. L., Giuliano, A.J., Meyer, A.C., **Addington, J.**, Cadenhead, K.S., Cannon, T.D., McGlashan, T., Perkins, D.O., Tsuang, M.T., Walker, E.F., Woods, S., Bearden, C.E., Christensen, B.K., Hawkins, K., Heaton, R., Keefe, R.S.E., Heinssen, R., Cornblatt, B.A. (2010) Neuropsychology of the Prodrome to Psychosis in the NAPLS Consortium: Relationship to Family History and Conversion to Psychosis. *Archives of General Psychiatry*, 67, 578-588
9. Cadenhead, K.S., **Addington, J.**, Cannon, T.D., Cornblatt, B.A McGlashan, T., Perkins, D.O., Seidman. L., Tsuang, M.T., Walker, E.F., Woods, S., & Heinssen, R. (in press) Treatment History in the Psychosis Prodrome: Characteristics of the North American Prodrome Longitudinal Study Cohort. *Early Intervention in Psychiatry*
10. **Addington, J.**, & Piskulic, D., (in press) Social cognition and functional outcome are separate domains in schizophrenia. *Schizophrenia Research*,

#### **Book Chapters**

1. **Addington, J.**, Mancuso E., Haarmans, M. ( in press). Cognitive Behaviour Therapy and Early Intervention. In Douglas Turkington, Roger Hagen, Torkil Berge & Rolf.W.Gråwe (Eds.), *The CBT treatment of psychosis - a symptomatic approach* (chapt. 7). Routledge.
2. McGorry PD & **Addington J.**, (in press) Detection and Management of Early Psychosis in J.A. Lieberman & R.M. Murray (eds) *Comprehensive Care of Schizophrenia: A textbook of clinical management* (2<sup>nd</sup> Edition) Oxford University Press.

#### **Published Abstracts**

1. Mizrahi, R., **Addington, J.**, Rusjan, P., et al., (2010) Stress-induced dopamine release in subjects at clinical high risk for psychosis and in antipsychotic naive patients with psychosis: A [11c]-(+)-PHNC PET study. *Schizophrenia Research*, 117, 173-4.
2. Jones, E., Trotmam, H., Esterberg, M.L., Brasfield, J., Walker, E.F., **Addington J.**, et al., (2010) Prodromal symptoms: differential effects of sex and family history. *Schizophrenia Research*, 117, 197.
3. **Addington, J.**, Cornblatt, B.A., Cadenhead, K.S, Cannon, T.D, Heinssen, R., McGlashan, T.H., Perkins, D.O., Tsuang, M.T., Walker, E.F., Woods, S.W., & Seidman L.J. (2010) Attenuated Psychotic Symptoms: The risk of false positive. *Schizophrenia Research*, 117, p279.

4. Holtzman, C.W., Larson, M.K., **Addington, J.**, et al., (2010) Sex differences in symptom presentation in individuals at risk for psychosis. *Schizophrenia Research*, 117, p304-5
5. Piskulic, D., **Addington, J.**, Auther, A., & Cornblatt, B.A. (2010) Using the Global Functioning Social and Role Scales in a First Episode Sample. *Schizophrenia Research*, 117, p406.
6. Piskulic, D., **Addington, J.**, & Maruff, P., (2010) Social Cognition in Schizophrenia: A quantitative review of the literature. *Schizophrenia Research*, 117, p413-414.
7. Piskulic, D., & **Addington, J.**, (2010) Social cognition and functional outcome are separate domains in schizophrenia. *Schizophrenia Research*, 117, p528
8. Seidman, L., Giuliano, A.J., Meyer, A.C., **Addington, J.**, Cadenhead, K.S., Cannon, T.D., McGlashan, T., Perkins, D.O., Tsuang, M.T., Walker, E.F., Woods, S., Bearden, C.E., Christensen, B.K., Hawkins, K., Heaton, R., Keefe, R.S.E., Heinssen, R., Cornblatt, B.A. (2010) Neuropsychology of the Prodrome to Psychosis in the NAPLS Consortium: Relationship to Family History and Conversion to Psychosis. *Schizophrenia Research*, 117, p176

#### **Invited Plenary Lectures**

1. Clinical High Risk for Psychosis: Research or Clinical Practice. Presentation at Child & Adolescent Psychiatry CME Rounds, September 10<sup>th</sup>, 2009
2. "Models and impact of substance abuse on the clinical course and outcome of patients with a first episode of psychosis" 7<sup>th</sup> International Meeting on the Early Phases of Mental Illness: Outcome in First Episode Psychosis. Santander, Spain 12-14 November 2009
3. "Clinical course and outcome of after discharge from and early intervention program of first episode psychosis" 7<sup>th</sup> International Meeting on the Early Phases of Mental Illness: Outcome in First Episode Psychosis. Santander, Spain 12-14 November 2009
4. Clinical High Risk for Psychosis: Research and Clinical Practice. Presentation at The Faculty of Health Sciences, University of Lethbridge, January 22<sup>nd</sup>, 2010
5. Early Detection and Intervention for those at Clinical High Risk for Psychosis. Grand Rounds, Department of Psychiatry, University of Calgary, February 26<sup>th</sup> 2010
6. Early Detection and Intervention for those at Clinical High Risk for Psychosis. Schizophrenia Research Group, University of Oslo, Norway March 4<sup>th</sup> 2010
7. The importance of education campaigns in the early detection of psychosis, presentation at doctoral thesis defence, Stavanger, Norway, April 30<sup>th</sup> 2010

8. At Clinical High Risk for Psychosis – what is the outcome?. Paper presented at the American Psychiatric Annual Meeting, New Orleans, May 24<sup>th</sup> 2010