Marc-André Roy, MD, FRCPC
Associate Professor, Department of Psychiatry and Neurosciences, Université Laval and CERVO research center
Medical Director, CNDV
Québec, Québec

Phil Tibbo, MD, FRCPC
Dr Paul Janssen Chair in Psychotic Disorders
Director, Nova Scotia Early Psychosis Program
Professor, Department of Psychiatry
Dalhousie University, Halifax, Nova Scotia
Workshop Objectives

• After attending this workshop, participants will be able to:
  • Compare their practice patterns for the selection of clozapine and long-acting injectable (LAI) antipsychotic treatment in early phase psychosis to a national benchmark
  • Identify patients in their practice who could benefit from a systematic approach to antipsychotic treatment selection
  • Apply an evidence-based clinical order set for the initiation of antipsychotic treatment in the early phase of illness
Canadian Consortium for

Early Intervention in Psychosis

Clozapine Use in Canadian Early Intervention Programs

Marc-André Roy, MD, FRCP
CNDV/Université Laval, Québec
(on behalf of CCEIP)
Disclosures: Marc-André Roy, MD, FRCP

- Research Support: IRSC, FRQ-SC, Janssen, Mylan, Otsuka-Lundbeck
- Paid Speaker: Janssen, Mylan, Otsuka-Lundbeck
- Consultant: Janssen, Otsuka-Lundbeck
Objectives

• To review potential benefits of Clozapine use in early intervention
• To examine its current use in early intervention programs across Canada
• To provide preliminary data on patterns of use and impact of Clozapine in early psychosis patients
## Positive Outcomes with Clozapine

### Positive Outcomes Include:

<table>
<thead>
<tr>
<th>Outcome</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Virtually no EPS or TD</td>
<td>Meltzer HY, et al. Arch Gen Psychiatry; 2003, 60(1):82-91.</td>
</tr>
<tr>
<td>Adherence to treatment</td>
<td></td>
</tr>
</tbody>
</table>
Positive Outcomes with Clozapine

**Positive Outcomes Include:**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lower mortality rate compared to other antipsychotics</td>
<td>De Hert M, et al. Schizophr Res 2010;117:68-74.</td>
</tr>
</tbody>
</table>

*These outcomes are particularly relevant for early intervention!*
Does This Translate in Early Intervention?  
An Algorithm-Based Approach to First-Episode Schizophrenia

Outcome for Treatment Algorithm in Patients (n=327)  
With DSM-IV First-Episode Schizophrenia or Schizoaffective Disorder

**Treatment algorithm offered**  
(n = 327)  

**Available for assessment**  
(n = 287)  

**Trial 1**  
Olanzapine (n = 140, 57.4%)  
or  
Risperidone (n = 104, 42.6%)  
(n = 244)

**Trial 2**  
Olanzapine (n = 35, 58.3%)  
or  
Risperidone (n = 25, 41.7%)  
(n = 60)

**Trial 3**  
Clozapine trial (n = 28, 56%)  
or  
Continuation of trial (n = 22, 44%)  
(n = 50)

**Declined treatment, unable to complete one antipsychotic trial, or started on antipsychotic other than olanzapine or risperidone (n = 43)**

**Responders (n = 184, 75.4%)**  
Olanzapine (n = 115, 82.1%)  
Risperidone (n = 69, 66.3%)

**Responders (n = 10, 16.7%)**  
Olanzapine (n = 9, 25.7%)  
Risperidone (n = 1, 4.0%)

**Clozapine responders (n = 21, 75.0%)**  
Continuation responders (n = 0, 0%)

Abbreviation: *DSM-IV* = Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition

Is Clozapine Underutilized?

• Horvitz-Lennon et al, 2009
  • Underuse of Clozapine: one of the most conspicuous examples of a lack of attention to evidence-based medicine

• Variations in use:
  • New Zealand:
    • Outpatients with schizophrenia: 917/2796 (32.8%) are on Clozapine;
    • 18% of EPI patients were started in two years or less from first initiation of antipsychotic and 19% in years 3-5
  • Canada: very low rate of Clozapine use!
    • < 7% of patients with schizophrenia are on Clozapine

Is Clozapine Underutilized?

- Horvitz-Lennon et al, 2009
  - Underuse of Clozapine: one of the most conspicuous examples of a lack of attention to evidence-based medicine

Variations in use:
- New Zealand:
  - Outpatients with schizophrenia: 917/2796 (32.8%) are on Clozapine;
  - 18% of EPI patients were started in two years or less from first initiation of antipsychotic and 19% in years 3-5

- Canada: very low rate of Clozapine use!
  - < 7% of patients with schizophrenia are on Clozapine

Recent Meta-analysis of Antipsychotics in TRS (Samara et al, JAMA Psy 2016)

• 40 RCTs (n=40) in TRS; total n=5172
• Efficacy rankings:
  • Olanzapine > Quetiapine, Haloperidol, Sertindole
  • Clozapine > Haloperidol, Sertindole
  • Risperidone > Sertindole
• Insufficient evidence to support superiority of Clozapine to other second generation APs

Recent Meta-analysis of Antipsychotics in TRS (Samara et al, JAMA Psy 2016)

- 40 RCTs (n=40) in TRS; total n=5172
- Efficacy rankings:
  - Olanzapine > Quetiapine, Haloperidol, Sertindole
  - Clozapine > Haloperidol, Sertindole
  - Risperidone > Sertindole
- Insufficient evidence to support superiority of Clozapine to other second generation APs

Possible Methodological Explanation

Kane and Correll, 2016:
• Increasing placebo effect over last decades
• Variations in definitions of treatment-refractoriness
• Variations in documenting prospective trials before inclusion in studies
• Insufficient Clozapine dose
• Possible unblinding (e.g., differences in side-effects profiles)
Possible Methodological Explanation

Kane and Correll, 2016:

• Increasing placebo effect over last decades

“...our first reaction is how unfortunate it is that our field still struggles with this question more than 25 years after the 1988 publication by Kane et al led to the introduction of clozapine into clinical care in the United States...”
HOW MUCH IS CLZ USED IN CANADIAN PEPP?

CCEIP National Survey: Clozapine Use

- Survey of 11 programs from Canadian Consortium for Early Intervention in Psychosis (CCEIP)
- Total number of patients = 1771, range per program from 45 to 392
- Various settings (academic vs. non-academic, from large metropolitan areas to rural settings)
Further investigation of the sources of heterogeneity revealed more frequent use in programs:

- Using a systematic algorithm to assess treatment resistance (17.2% vs. 10.6%)
- With dedicated hospital beds (18.0% vs. 9.5%)
- With a program follow up longer than two years (14.8% vs. 6.2%)
Mean rate of use = 13.5%
95% confidence of the mean = 7.1%, 19%
Highly significant heterogeneity ($X^2 : p < 0.0001$)
Retrospective Chart Audit on Use of Clozapine – Inclusion/ Exclusion Criteria

• Three participating centres: Dalhousie, Laval, University of Victoria

• Patients consecutively admitted to either program followed for ≥ 3 years (n = 147)

• Aged between 18-30 years old at some time during this three year follow-up

• DSM-5 diagnosis of:
  • Schizophrenia (n = 96)
  • Schizoaffective disorder (n = 18)
  • Schizophreniform disorder (n= 3)
  • Delusional disorder (n= 6)
  • Psychosis NS (n= 24)

• Patients with mood-disorders, drug-induced psychotic disorder or psychotic disorder due to a medical condition were excluded
### Methods

- Retrospective chart review
- For each antipsychotic trial:
  - Dosage, duration and adherence were recorded
  - CGI-S once the medication was clinically judged as optimal was rated
  - Patients were considered:
    - Fully remitted when CGI-S ≤ 3 (mild, borderline or normal)
    - Partially remitted when CGI-S = 4 (moderate)
    - Not remitted when CGI ≥ 5
## Demographics

<table>
<thead>
<tr>
<th>Population (n=147)</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender</strong></td>
<td>118 males, 29 females</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Mean age at program inclusion</strong></td>
<td>21.7 (sd 3.2)</td>
<td>3.2 (sd)</td>
<td>17-30</td>
</tr>
<tr>
<td><strong>Mean age at chart review</strong></td>
<td>26.5 (sd 3.9)</td>
<td>3.9 (sd)</td>
<td>21-36</td>
</tr>
<tr>
<td><strong>Age at program inclusion</strong></td>
<td>21.7 (sd 3.2)</td>
<td>3.2 (sd)</td>
<td>17-30</td>
</tr>
</tbody>
</table>
# Comorbidities

<table>
<thead>
<tr>
<th>Psychiatric</th>
<th>Physical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Substance use disorder</td>
<td>Diabetes</td>
</tr>
<tr>
<td>100 (68%)</td>
<td>1 (0.7%)</td>
</tr>
<tr>
<td>Anxiety disorder</td>
<td>Dyslipidemia</td>
</tr>
<tr>
<td>46 (31%)</td>
<td>16 (11%)</td>
</tr>
<tr>
<td>OCD</td>
<td>Hypertension</td>
</tr>
<tr>
<td>6 (4%)</td>
<td>7 (5%)</td>
</tr>
<tr>
<td>Major depressive disorder</td>
<td>Obesity</td>
</tr>
<tr>
<td>23 (16%)</td>
<td>6 (4%)</td>
</tr>
<tr>
<td>Post traumatic stress disorder</td>
<td>Hypothyroidism</td>
</tr>
<tr>
<td>6 (4%)</td>
<td>5 (3%)</td>
</tr>
<tr>
<td>Personality disorder</td>
<td>Hyperprolactinemia</td>
</tr>
<tr>
<td>13 (9%)</td>
<td>3 (2%)</td>
</tr>
<tr>
<td>ADHD</td>
<td>Others</td>
</tr>
<tr>
<td>22 (15%)</td>
<td>22 (15%)</td>
</tr>
<tr>
<td>Others</td>
<td>None</td>
</tr>
<tr>
<td>8 (5%)</td>
<td>93 (63%)</td>
</tr>
<tr>
<td>None</td>
<td></td>
</tr>
</tbody>
</table>
115/147 patients (78%) had reached full remission during the chart review interval.

More than half of them (63/115; 54%) in the first AP trial.

At the end of the chart review interval, 110/147 (75%) patients were still in full remission.
Proportion of Patients Reaching Full Remission by Antipsychotic Trial Rank

% (n) of pts reaching full remission

- First AP trial: 43% (n=63)
- Second AP trial: 15% (n=22)
- Third AP trial: 14% (n=21)
- Fourth AP trial: 5% (n=7)
- Fifth AP trial or more: 1% (n=2)
Trial 1:
Risperidone (43%) > Olanzapine (21%) > Quetiapine (19%) > others
Use of LAIs (9%)
No clozapine

Trial 2:
Paliperidone (25%) > Aripiprazole (23%) > Quetiapine (19%) > others
Use of LAIs (12%)
No clozapine

Trial 3:
Clozapine (32%) > Aripiprazole (29%) > Paliperidone (14%) > others
Use of LAIs (9%)
LAI

- Globally, 59/147 (40%) patients were exposed to LAIs

Clozapine

- Globally, 29/147 (20%) patients were exposed to clozapine after a mean of 2.89 AP trials
## Patients Not in Full Remission Who Were Not Prescribed Clozapine (n = 28)

<table>
<thead>
<tr>
<th>Reasons why Clozapine was not introduced (more than one reason can applied)</th>
<th>N*</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Option never considered</td>
<td>5</td>
<td>20%</td>
</tr>
<tr>
<td>Major medical contraindication</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Residual symptoms considered non-severe</td>
<td>5</td>
<td>20%</td>
</tr>
<tr>
<td>Major medication adhesion problems anticipated</td>
<td>8</td>
<td>32%</td>
</tr>
<tr>
<td>Patient refusal</td>
<td>1</td>
<td>4%</td>
</tr>
<tr>
<td>Organisation of care incompatible with clozapine follow-up</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Major substance use disorder</td>
<td>6</td>
<td>24%</td>
</tr>
<tr>
<td>Others</td>
<td>2</td>
<td>8%</td>
</tr>
<tr>
<td>Missing reasons</td>
<td>1</td>
<td>4%</td>
</tr>
</tbody>
</table>
### Reasons Why Clozapine Was Offered

<table>
<thead>
<tr>
<th>Reason</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insufficient response to previous trials</td>
<td>28 (96.6)</td>
</tr>
<tr>
<td>EPS with previous drugs</td>
<td>6 (20.7)</td>
</tr>
<tr>
<td>Severe impulsivity</td>
<td>2 (6.9)</td>
</tr>
<tr>
<td>Substance use disorder</td>
<td>9</td>
</tr>
<tr>
<td>Suicide risk</td>
<td>4</td>
</tr>
<tr>
<td>Violence</td>
<td>4</td>
</tr>
</tbody>
</table>

- Total remission was reached on clozapine for 20/29 (69%) patients
- Partial remission was reached in 9/29 (31%) of exposed patients
Clozapine Pattern of Use

- Clozapine was initiated on an outpatient setting in 55% of cases
- 8/29 were previously treated with a LAI
- In the clozapine exposed group, in comparison to the others:
  - More patients were on CTO or extended leave (41 vs 28%, respectively),
  - More patients had a comorbid substance use disorder (83 vs 64%), and,
  - More personality disorder (21 vs 6%, respectively)
• Dose range from 150 to 600 mg daily,
  • Modal dose 400 mg

• Once daily regimen was used in 2/3 of cases

• Blood levels were used in 26/29 (90%) of patients
Limitations

- Modest sample size
- Retrospective ratings
- Under-reporting of comorbidities
Conclusions

- Clozapine is more widely used in early intervention programs than would be typically assumed
- Clozapine may be introduced in an outpatient setting
- It can be in some instances successfully used patients with a typical non-adherent profile
- Rates of response may be particularly high in this population
Canadian Consortium for Early Intervention in Psychosis

Long-Acting Injectable Antipsychotic (LAI) Use in Canadian EPI Services: CCEIP National Survey Results

Dr Philip Tibbo
The Canadian Consortium for Early Intervention in Psychosis (CCEIP)

National, not-for-profit physician organization of clinicians and researchers dedicated to improving the quality of care for individuals suffering from psychotic disorders in the early stages.

We have 30 members across Canada.
Background

• An earlier Canadian study (Williams et al 2006) found the overall rate of LAI use low in Canada compared to other parts of the world.

• Members of the Canadian Consortium for Early Intervention in Psychosis (CCEIP) published the Canadian Recommendations for the Use of LAIs in 2013.

• Since the CCEIP recommendations were published, the extent of use of LAIs has been based on data available to industry.
  • Research question: Has there been a change in rates of use in EIS for psychosis since the introduction of SGA LAIs and the publication of the Canadian Recommendations?
Canadian Working Group’s Recommendations

- **Canadian Recommendations for the Use of Long-Acting Injectables:**

  Greater use of LAIs, especially during early course of psychotic disorders, may prevent relapses in vulnerable patients, prolong periods of remission, and facilitate engagement in psychosocial interventions and rehabilitation in patients otherwise unlikely to engage in these aspects of treatment.

Early Data

- Preliminary work (as part of another study) by CCEIP with 10 academic EIS programs in Canada (1,555 EIS subjects; 71% male) showed an overall LAI use rate of 31% and aggregate rate of use in the first year of illness of 23%
  - “Preliminary exploration of the current use of long-acting injectable antipsychotics in Canadian early intervention services for psychosis.”
    
    Philip G. Tibbo, Amelie Achim, Ashok Malla, Nicola Banks, Marc-Andre Roy (IEPA 2016, Milan)

- However, the preliminary survey was not comprehensive nor specific to LAIs; so a second, more detailed national survey was conducted during summer/fall of 2016
2016 Canadian EIS LAI Use Survey

• Unique respondents from Early Intervention Services (EIS)
  • 13 CCEIP members
  • 8 non-CCEIP members

• 3 survey responses were excluded for failing to meet the inclusion criteria of reporting number of active patients and number on LAIs

• Survey was detailed for program demographics, LAI use total and per year (gender/CTO/ethnicity), administration, treatment specifics

• Analysis conducted on 18 surveys which comprised data on 2448 individuals
The population served by each program were self-identified:

- 9 urban
- 4 suburban
- 2 mixed
- 3 rural
Location:

- 11 located in a hospital
  - 3 academic psychiatric
  - 6 academic general
  - 2 general hospital

- 7 located in the community
  - 2 identified as stand alone
  - 5 were located in a general mental health clinic
Duration of EIS Programs

Number of Programs

Program (years)

- <1
- 1
- 2
- 3
- 4
- 5
- Not fixed

Number of Programs:

- 0
- 1
- 2
- 3
- 4
- 5
- 6
- 7
- 8

Not fixed programs were not included in the count.
• 16 of 18 programs responded regarding ethnicity
• 1 program did not record ethnicity
• Respondents of each program were asked to profile ethnicity into 16 groups based on Stats Canada ethnic categories

Ethnicity of Populations Served

Arab
Black
Chinese
Filipino
First nations
Inuk
Japanese
Korean
Latin American
Metis
South Asian
Southeast Asian
West Asian
White
Unknown
Other
Reported LAI Use

- The overall reported percentage of LAI use across all 18 centers was **25.5 % +/- 13 (SD)**
- The level of use varied from a minimum of 5% to a maximum of 50%
Reported Prevalence of LAI Use – Profile of all Respondents
Thirteen centers reported that within the total LAI use that the average use of LAIs associated with Community treatment orders (CTO) was 21% +/- 20 (SD).

It was noted in the responses that not all regions have CTOs or extended leave provisions available to them.

LAI use under CTO was more common for males (83% +/- 16) versus females (17% +/- 16).

Within this population, no use under CTO/extended leave was reported by transgendered individuals.
LAI Use Based on Population Density

• There were no significant differences between groups divided by population density

• The greatest variability in responses was seen in the rural grouping, but the sample was too small to draw firm conclusions
Gender and LAI Use

• In the total EIS patient population:
  • 67 +/- 15% were male,
  • 32 +/- 13 % were female, and
  • 1 +/- 2 % were transgendered (average +/- SD)

• Among patients using LAIs:
  • 76 +/- 23% were male,
  • 27 +/- 22% were female, and
  • 0.3 +/- 0.9% were transgendered (average +/- SD)
First Generation Antipsychotics vs Second Generation Antipsychotics

- There was a significant difference between use of First Generation Antipsychotics (FGA) and Second Generation Antipsychotics (SGA) LAIs (p<0.001)
The rate of LAI use was essentially unchanged over the years of illness at 29, 24, and 27% respectively for the first, second and third years of illness as defined by “within the ‘x’ year with your EPI program” 

12 sites responded to this section
• On average, **patients were hospitalized 1.4 +/- 0.5 (SD) times prior to beginning on LAIs** (n=14). It was noted by one respondent that their hospital will not start LAIs.

• On average, **patients experienced 1.5 +/- 0.5 (SD) relapses prior to starting LAIs** (n=13).
Switching from LAI

• The survey asked: “Approximately how many of your EPP patients have been switched from an LAI back to an oral formulation in the last year?”

• With 13 of 18 clinics responding, a total of 40 patients were reported to have been switched

• This is in comparison to a total of 458 patients on LAIs for these same responding clinics
How are the Injections Administered?

• The survey asked: "Who gives the injection to your patients at your EPI program? Please select all that apply":
  • 11 of 13 used EPI-Nurse
  • 4 of 13 used Psychiatric Nurse outside of EPI program
  • 2 used Community Nurses
  • 1 used General Practitioner
  • 1 used Nurse Practitioner

• 9 of 14 EPI clinics (64%) performed injections on site
n=12, values at the top of each bar indicate the total number of patients receiving each medication.
Evaluation Tools for Medication Side Effects

Evaluation Tools and Their Frequency of Use

AIMS was the most commonly administered tool at all time points.
What factors drive deviation from the average starting dosage?

Side effect profiles were cited as the main driver affecting initial dose choices followed by severity of illness considerations.

In other reasons given, ethnicity was cited as well as patient preference, last used dose of oral, drug interactions and co-morbid substance abuse.
LAI Use in EIS for Psychosis in Canada

Discussion and Questions
Disclosures: HC Margolese MD, FRCPC

• Research Support: Boehringer-Ingelheim, Janssen, Lundbeck, Otsuka

• Paid Speaker: BMS, Janssen, Lundbeck, Otsuka, Sunovian

• Consultant: BMS, Janssen, Lundbeck, Otsuka, Pfizer, Shire, Sunovian
A CCEIP Focus

- Create NATIONAL standards of care for early intervention in psychosis
- Integrate best practices into clinical workflow (clinical tools)
- Evaluate impact of knowledge translation activities

Clinical Order Sets
Hand-written Orders

• No treatments are provided to patients in hospitals without a doctor’s order

• A doctor will hand write treatment instructions on a blank order page and submit to nurse for execution
  • Time consuming
  • Very prone to error
  • Practice variation
What is a Clinical Order Set?

- A pre-defined template that provides support in making clinical decisions for a specific condition or medical procedure
- A grouping of orders that standardizes and expedites the ordering process for a common clinical scenario
- Clinical order sets guide clinicians while treating patients to ensure that they do not miss any critical components of care
- Order sets can be used to incorporate the latest evidence-based best practice to clinical workflow
Advantages of Clinical Order Sets

- Aligned to provincial mandates (HQO Schizophrenia Care Standard)
- Reduces variability
- Integrates best practices (standardized approach)
- Identifies practice patterns
- Facilitates outcome evaluations
- Can be customized based on existing policies and procedures and to reflect variances in practice
- Can be integrated into Electronic Medical Records
In partnership with Think Research, we are developing and testing two clinical order sets:

1. Initiation of Treatment for Early Phase Psychotic Disorders

2. Optimization of Treatment for Early Phase Psychotic Disorders
Order Set Themes

- **Administration**
  - Document Purpose
  - Working Diagnosis

- **Substance Use Screening**
  - Alcohol Use Disorders Identification Test (AUDIT)
  - Drug Abuse Screening Test, DAST-10

- **Additional Information**

- **Psychiatric Symptoms Assessment Tools**
  - Clinical Global Impression-Severity (CGI-S) Scale
  - Brief Psychiatric Rating Scale (BPRS) 4-Item Positive Symptom Rating Scale
• **Physical Assessment**
  - Movement Disorder Assessment Tools
    - Tools for Monitoring Antipsychotic Side Effects (TMAS)
    - Abnormal Involuntary Movement Scale (AIMS)
    - Extrapyramidal Symptom Rating Scale (ESRS)
  - Vitals/Monitoring
  - Lab Investigations (if not previously obtained)
  - Diagnostics

• **Allergies and Medication Review**

• **Antipsychotic Treatment Capacity Assessment**
• **Management of Psychosis**
  - It is recommended that preference be given to atypical antipsychotics in the treatment of early psychosis patients
  - It is recommended that LAI (Long-Acting Injectable) antipsychotic therapy is offered during all phases of psychotic disorders, including the early phase
  - To address high rates of partial/non-adherence in early psychosis patients, preference is given to medications available in a long acting formulation
  - Refer to Antipsychotic Treatment Selection Tool

• **Atypical Antipsychotics**
  - Oral Medication with LAI Formulations
  - LAI Antipsychotic Medication
  - OR
  - Alternate Atypical Antipsychotic Medication
  - Patient choice; refer to OPTIMA: Offering Patients Therapeutic Information on Medication Alternatives
Order Set Themes (con’t)

- **Adjunctive Management**
  - Anticholinergic Agents
  - Benzodiazepines
  - Other

- **Cognitive Behavioural Therapy**

- **Smoking Cessation**

- **Psychoeducation and Health Lifestyle Information**
  - Provide psychoeducation to patient, refer to iHope tool

- **Referrals**

- **Additional Orders**
Initiation of Treatment for Early Phase Psychotic Disorders Order Set

<table>
<thead>
<tr>
<th>Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Document Purpose</strong></td>
</tr>
<tr>
<td>This order set may be used for adult patients in both inpatient and outpatient care settings.</td>
</tr>
<tr>
<td>An ‘adequate trial of antipsychotic medication’ for the purpose of this document considers adequacy in terms of dose, duration, and effectiveness.</td>
</tr>
<tr>
<td><strong>Duration:</strong> oral antipsychotic medication trial for at least 6 weeks, or long acting injectable (LAI) antipsychotic for at least 4 8-week cycles</td>
</tr>
<tr>
<td><strong>Efficacy assessment:</strong> at least 70% of the time</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Working Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dimension based on criteria from the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5)</strong></td>
</tr>
<tr>
<td>Select one:</td>
</tr>
<tr>
<td>- Unspecified Schizophrenia Spectrum and Other Psychotic Disorder</td>
</tr>
<tr>
<td>- Schizophrenia</td>
</tr>
<tr>
<td>- Schizoaffective Disorder</td>
</tr>
<tr>
<td>- Bipolar spectrum disorder</td>
</tr>
<tr>
<td>- Mood Disorder</td>
</tr>
<tr>
<td>- Delusional Disorder</td>
</tr>
<tr>
<td>- Other (specify)</td>
</tr>
<tr>
<td>- Comorbid Diagnoses (Medical and Psychiatric)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Substance Use Screening</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Screen for substance use:</strong></td>
</tr>
<tr>
<td>- Clinical interview</td>
</tr>
<tr>
<td>- Validated screening tool</td>
</tr>
<tr>
<td>- Alcohol Use Disorders Identification Test (AUDIT)</td>
</tr>
<tr>
<td>- Self-report</td>
</tr>
<tr>
<td>- Clinician guided</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Additional Information</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Obtain collateral information from:</strong></td>
</tr>
</tbody>
</table>

---

**Reference:** Document title: Initiation of Treatment for Early Phase Psychotic Disorders Order Set. Document purpose: This order set may be used for adult patients in both inpatient and outpatient care settings. A ‘adequate trial of antipsychotic medication’ for the purpose of this document considers adequacy in terms of dose, duration, and effectiveness. Duration: oral antipsychotic medication trial for at least 6 weeks, or long acting injectable (LAI) antipsychotic for at least 4 8-week cycles. Efficacy assessment: at least 70% of the time. Working diagnosis: Dimension based on criteria from the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5). Substance use screening: Screen for substance use. Additional information: Obtain collateral information from.
Initiation of Treatment for Early Phase Psychotic Disorders Order Set (con’t)

Psychiatric Symptoms Assessment Tools

- Clinical Global Impression-Severity (CGI-S) Scale
- Consider your clinical impression with this particular population, how mentally ill is the patient at the time?
- Select one:
  - 1 = Normal
  - 2 = Borderline mentally ill
  - 3 = Mildly ill
  - 4 = Moderately ill
  - 5 = Severely ill
  - 6 = Among the most extremely ill patients

- Brief Psychiatric Rating Scale (BPRS) 18-Item Positive Symptom Rating Scale available at:

Physical Assessment

Movement Disorder Assessment Tools

- Tools for Monitoring Antipsychotic Side Effects (TAMAS)
- Available at: [Link]
- Normal Movement Scale (NMAS) available at: [Link]
- Fetrantipiride Symptom Rating Scale (FRSRS)

Vital Signs

- Weight: [Weight] kg
- Height: [Height] m
- BMI: [BMI] kg/m²
- Pulse: [Pulse] bpm
- Blood Pressure: [Blood Pressure]

Lab Investigations (if not previously obtained)

Chemistry

- Electrolytes (Na⁺, K⁺, Cl⁻, HCO₃⁻)
- Creatinine
- ALT
- Protein

Additional Lab Investigations

- Fasting glucose
- HbA1C
- HDL, LDL, Total Cholesterol, Triglycerides

Subscribed by: ________________________________

Reviewed by: ________________________________
Initiation of Treatment for Early Phase Psychotic Disorders Order Set (con't)

Physical Assessment Continued...

Diagnostics
- CT
- MRI
- EEG
- Reason:

Allergies and Medication Review
Allergies (list allergens and reactions):

Medication Review
- Complete an assessment of current and past medication trials
- Document known current or ontolosophical trials and trials:
  - Adherence:
  - Reason for discontinuation:
  - Adherence:
  - Side Effects:
  - Reason for discontinuation:
  - Reason:

Antipsychotic Treatment Capacity Assessment
- Low:
- Acceptable, as per local capacity definition/requirements
- Further treatment capacity assessment may be required

Submitted by:
- Read Back
- Date:
- Initials:

Reference: Document Only
### Initiation of Treatment for Early Phase Psychotic Disorders Order Set (con’t)

**Adjuvant Management Continued…**

<table>
<thead>
<tr>
<th>Combination</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antidepressants</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td></td>
</tr>
</tbody>
</table>

**Cognitive Behavioural Therapy**

- Is patient appropriate for cognitive behavioural therapy (CBT)?
  - Yes
  - No
  - Further assessment required
  - If patient appropriate for CBT and CBT not offered, please provide explanation (e.g., patient refusal).

**Smoking Cessation**

- Pharmacological treatment considered, using counseling more effective than pharmacological treatment alone.
  - Yes
  - No
- If patient a smoker, offer smoking cessation education and interventions. Please provide explanation (e.g., patient refusal).

**Pharmacological Management**

- Nicotine patch: 
  - Specify mg
  - Topically for 
  - weeks, then notify MDPD to reassess (14 – 21 mg)

**Psychoeducation and Health Lifestyle Information**

- Provide education to patient on the following topics: verbally, in writing, and electronically, as applicable:
  - Side effects
  - Treatment options, including their potential efficacy and side effects
  - Address treatment options, including counseling
  - Risk of relapse and recognition of warning signs and relapse prevention strategies
  - Risk of suicide and following for warning signs
  - Impact of substance use (particularly cannabinoids), including intervention if treatment options as well as illness
  - Importance of adherence with treatment and follow-up as well as adherence enhancement strategies

- Offer family intervention to provide family focused psychoeducation and support:

**Prescribe to initiate referral to Smoking Cessation Counselor in the Referral section, as appropriate**

---

**Author:**

**Date:** 11/7/17
Initiation of Treatment for Early Phase Psychotic Disorders Order Set (con't)

<table>
<thead>
<tr>
<th>Referrals</th>
<th>ACTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBT</td>
<td>Individual</td>
</tr>
<tr>
<td>Concurrent Interventions: Treatment</td>
<td>Reason</td>
</tr>
<tr>
<td>Family Intervention</td>
<td>SW</td>
</tr>
<tr>
<td>OT</td>
<td>Reason</td>
</tr>
</tbody>
</table>

Additional Orders

---

Submitted by: [Signature]
Date: [Date]

Read Back: [Signature]
Date: [Date]
Initiation of Treatment for Early Phase Psychotic Disorders Order Set (con’t)

### Implementation Considerations

- **Obesity and Antipsychotics**: This order set reflects the general preference toward initiation of antipsychotics in obese patients. Consider selective use of antipsychotics to reduce weight gain and improve clinical outcomes.
- **Diagnostic Imaging**: Routine use of neuroradiographics in first-episode psychosis may not yield additional diagnostic information that would alter clinical management in a meaningful way.
- **Electroconvulsive Therapy (ECT)**: Consider ECT for patients with severe, treatment-resistant psychosis or when there is a high risk of suicide.
- **Discharge Planning**: Cease antipsychotic medications when a patient is discharged from the hospital. However, ongoing care may be required for patients with ongoing psychotic symptoms.
- **Drug Specific Reminders**: Advise patients to start antipsychotic medications and review at each visit.

### References

**Key references:**


Initiation of Treatment for Early Phase Psychotic Disorders Order Set (con't)


Dissemination Strategies

- EPION conference – May 15 – 19, 2017 (Toronto)
- CPA Workshop – September 14 – 16, 2017 (Ottawa)
- WPA Workshop – October 8 – 12, 2017 (Berlin)
- CCEIP Member Pilot – Summer 2017
- Association of General Hospital Psychiatric Services (AGHPS) Leadership Summit – November 2017 (Toronto)
- Think Research Network (13,000 users and admin)
- RCPSC Section 3 Accredited Program (Early 2018)
- Reaching out to other partner groups (e.g. AGHPS, EPION, national database of EPI clinics)
Canadian Consortium for Early Intervention in Psychosis

CCEIP Member Survey: Order Set Use
CCEIP Order Set Survey Results

- 7 provinces represented
- 22 responses, representing 19 clinics

N = 22
Does your site use clinical order sets?

Order Set Use

- Yes: 41%
- No: 50%
- Other: 9%

Comments

- Yes:
  - Not for medication ordering
  - We have a medication protocol ('safety first')
  - We use some order sets for initial bloodwork
  - Not mandatory. Although built into EMR, can override

- Other:
  - Very rare
  - We are developing one

N = 22
Who is responsible for the development and integration of clinical order sets at your site?

- **Clinicians (x10):**
  - Clinical coordinator
  - Clinical coordinator and clinic medical director
  - Clinicians including me together with the EMR development team
  - This was done collectively at least five years ago jointly by a number of clinicians (psychiatrists and non-psychiatrists)
  - It would be physician initiated and approved by managers
  - Developed by the team
  - Psychiatrist developed and implement

- **Regional health authority (x3):**
  - Regional Health Authority, quality department involved as well as clinical managers in the area
  - EPI Program/administration of regional health authority
  - Usually done by committee at health authority level

- **No one (x3):**
  - No one
  - No one in particular, the psychiatrists in our FEP team have regular clinical meetings where we talk about our practice
  - But we are working on similar projects.

- **Unclear at this point (x3)**

- **N/A (x1)**

\[N = 21\]
Does your site use an Electronic Medical Record (EMR) Platform?

**EMR Use**
- Yes: 64%
- No: 36%

**EMR Type**
- OACIS (x5)
- Accuro (x1)
- Cerner (icare) (x1)
- E-CLINICIAN (x1)
- Meditech (x1)
- PARIS (x1) (Not used for medication ordering)
- A local one (x1)
- Our clinical record is divided between Nightingale, OASIS and a paper medical administration record (MAR). We will be switching to EPIC over the next few years.
- Not indicated (x2)

N = 22
N = 11
Clinical order sets for EPI would be highly valuable.

I would be interested in the pilot implementing clinical order sets and would be willing to advocate within our health authority and hopefully provincially to implement.

Order sets at our site in use are not integrated but are paper based and include: 1) admission order set for psychiatry 2) order set for initiation of Paliperidone Palmitate

Hopefully the antipsychotic regimens promoted will not be in isolation from other important components of treatment.
• Clinical order sets for EPI would be highly valuable. Perhaps if as many sites as possible try to pilot this, the better. Some sites will have challenges with administration/hospital rules. I would try at my site, but am uncertain if there would be resistance or obstruction from managers.

• I would be interested in the pilot implementing clinical order sets and would be willing to advocate within our health authority and hopefully provincially to implement.

• Order sets at our site in use are not integrated with Meditech but are paper based and include: 1) admission order set for psychiatry 2) order set for initiation of Paliperidone Palmitate

• The safety first protocol is already available to CCEIP and can be and should be modified to include new developments, especially availability of new LAIs, new evidence produced by us and within the consortium on outcomes with aripiprazole (oral) in FEP (Schiz Research 2016) and new findings from Reliam study on AOM along with possibly other pieces of evidence on other antipsychotics. Hopefully the antipsychotic regimens promoted will not be in isolation from other important components of treatment.
Canadian Consortium for Early Intervention in Psychosis

Panel Discussion

Drs Roy and Tibbo
Thank you for attending

We encourage you to please complete the online evaluation @ www.cpa-apc.org/kiosk