Early Intervention for First Episode Psychosis

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Objectives

- Theory behind early intervention (EI)
- Concepts needed to analyze the First Episode Psychosis (FEP) literature
- Recovery After Initial Schizophrenia Episode (RAISE) trial
- Long term outcomes
- Future directions

Disclosure

No financial disclosures

RAISE trial Sub-1 and Prescriber
Navigate Certified Prescriber Trainer
Michigan Psychiatric Society President
CMH for Central Michigan Medical Director
National Council Medical Director Institute Member

Figure 1. Level of Recovery Achieved by Patients (N = 118) After Their First Episode of Schizophrenia or Schizoaffective Disorder

Cumulative Recovery Rate at 5-Year Follow-Up

*Data from Robinson et al.3

Phase of Illness

Premorbid  Prodrome  Acute   Plateau / Chronic

Most of the clinical and psychosocial deterioration occurs in first 5 years (Lambert et al. 2001).

Pragmatically important period: Symptom duration in first 2 years is strongest predictor of outcome (Lehman et al. 2006). Highest Suicide risk: Onset of substance misuse

Longer DUP associated with poorer outcomes (Lehman 2001)

Primary  Secondary  Tertiary Prevention

(Maher et al. & Rock City of Minnina, 2013)
Theory Behind EI- Stages of Illness

• Stage 0: Asymptomatic
• Stage 1A: Distress
• Stage 1B: Prodromal symptoms with sub-threshold specificity
• Stage 2: FEP
• Stage 3: Recurrent or Persistent
• Stage 4: Treatment Resistant

Relapse fuels the progression of illness

• With each relapse:
  ▪ Recovery can be slower and less complete
  ▪ More frequent admissions to hospital
  ▪ Illness can become more resistant to treatment
  ▪ Increased risk of self-harm and homelessness
  ▪ Regaining previous level of functioning is harder
  ▪ Patient has a loss of self-esteem and social and vocational disruption
  ▪ Greater use of healthcare resources
  ▪ Increased burden on families and caregivers

STOPPING MEDICATION IS THE MOST POWERFUL PREDICTOR OF RELAPSE

• Survival analysis: risk of a first or second relapse when not taking medication ~5 times greater than when taking it

![Graph showing hazard ratio for first and second relapse](image)
MP1  Please note, we have updated the reference details on this slide (we could not find this information in Olsson et al., Psychiatr Serv 2000).
Michelle Pelling-West, 7/18/2014
We tend to focus on what we don’t yet have in treatments

Maybe we should also focus on using better what we already have

White House Medicine Cabinet during the Madison administration

Reduce DUP and Treat Well

Development of Early Intervention for Psychosis in Australia

- 1986 - Dedicated Youth Psychosis ward at Aubrey Lew Unit
- 1992 – EPPIC established - Focus moved to the community and catchment area increased to 800,000. 24 hour crisis care, community care and research
- 1995 – PACE Clinic – ‘at risk’ for psychosis
- 1996 - 1st International conference on Early Psychosis
Types of Interventions in FEP Programs

- Early Detection (ED) initiatives to decrease DUP
  - Professional and general public education
  - Mobile crisis units
  - Rapid access to treatment
- Treatment is team-based and multidimensional
  - Low dose antipsychotics – standardized protocols
  - Therapy:
    - Individual and/or groups or classroom setting
    - Psychoeducation, CBT, Family
  - Vocational/Educational interventions
- Two years duration

Early Intervention Trials
Measuring Clinical Significance

- Response: Pre-determined % improvement from baseline
- Often set at a 20-25% decrease in total rating score (different than studies on depression)
- Cross-sectional measurement- no time component
- % may be set to best separate from intervention from placebo- may or may not correlate with significant clinical response

Early Intervention Trials
Measuring Clinical Significance

- Symptom Remission: (Andreasen et al 2005)
  - Minimal–mild on positive and negative symptoms on specific items in the SAPS and SANS
  - Items chosen related to 3 symptom dimensions:
    - Negative symptoms
    - Disorganization
    - Psychoticism or reality distortion
  - 6 months duration

- Functional Remission: (Robinson 2004)
  - Social Adjustment Scale
    - Appropriate role function- paid employment/school/homemaker
  - Ability to perform day to day activities without supervision
  - Social Interactions
  - Duration 2 years
Early Intervention Trials
Measuring Clinical Significance

• Recovery (Robinson 2004)
  – Symptom Remission
  – Functional Remission
  – Both of the above for a two year period

• Recovery: (Liberman et al 2005)
  – Stable Remission of both positive and negative symptoms
  – No psychiatric hosp or living in supported housing for the past 2 years
  – Currently engaged in work/study
  – GAF-F score greater than 60

OPUS- 10 year Outcomes
Summary

• Rates of remission and recovery relatively stable at years 2,5 and 10
• However, individual patients may go in and out of remission or recovery over time
• Of those recovered at Year 5, only 45 % were recovered at Year 10.
• Although 14% were recovered at Year 10, 30% achieved recovery at least once in the 10 years
Analyzing FEP Literature

- Definitions chosen
- Correlation with CGI
- Migration with time
- Detailed characteristics of EI
- Detailed characteristics of TAU

RAISE – ETP Site Distribution
34 sites in 21 states
**Shared Decision Making Skills**

- Facilitate active engagement in treatment
- Establish and maintain good working alliance between client and team members
- Support self-determination and personal autonomy
- Information provided about treatment options and likely consequences
- Client preferences elicited and respected
- Treatment decisions regulated and made jointly
- Family members involved (with client permission)

**Strengths and Resilience Focus**

- Identify personal qualities, knowledge, skills, and resources
- Draw attention to strengths, and consider how to capitalize on them to achieve goals
- Explore how person coped with and bounced back from previous challenges
- Build upon and enhance skills for dealing with stress and reboucing from setbacks

**Motivational Enhancement**

- Increase effort to work on personal goals
- Enhance client to improve illness management
- Resolve ambivalence about behavior change
- Help find a sense of purpose in life
- Empathic listening
- Elicit goals and support self-efficacy for achieving them
- Explore how improved illness management could help achieve goals
- Interventions for achieving goals

**Psychosocial Skills**

- Provide important information to assist shared decision-making
- Ensure relevant information is understood and received
- Facilitate access to information when needed
- Help individual learn practical facts about illness and its treatment
- Provide information in different formats (e.g., handouts, discussion, whiteboards)
- Break up information into small “chunks”
- Interactive teaching and discussion forms, with frequent feedback to ask and answer questions, check understanding, and explore person’s experience
- Adapt language, special terms (e.g., diagnosis), and amount of detail to the individual
- Seek common ground when there are disagreements about topics such as symptoms and diagnosis

**Family Collaboration Skills**

- Enlist family support for client goals and participating in treatment
- Improve monitoring of client’s disorder
- Reduce stress in the family
- Broad definition of “family” based on client’s wishes
- Outright suggest family members
- Provide information to family about illness and treatment
- Elicit and respond to family members’ questions and concerns
- Avoiding judgment and expressing empathy about challenging experiences
- Ensure that treatment team members are accessible to family
- Respond to family requests for help
- Information provided parallels much of the standard IRT work
- Resilience focus

**Mood Stabilizing (MIS)**

- Help classify permanent/mood goals
- Use biophysical treatment
- Focus on improving sleep disturbances
- Improve treatment management, including sleep patterns
- Relaxation techniques
- Increase or reduce use of mood stabilizers
- Improve mood
- Improve insight

**Psychiatric BN Intervention**

- Behaviorally based cognitive-behavioral therapy and individual therapy
- Family therapy
- Hospitalization counseled early for mood swings
- Individual and family motivational interviewing
- Family therapy and individual motivation
- Hospitalization and relapse prevention
- Family therapy and individual motivational interviewing
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- Family therapy and individual motivational interviewing
- Hospitalization and relapse prevention
- Family therapy and individual motivational interviewing
- Hospitalization and relapse prevention

**Standard Mnemonics**

<table>
<thead>
<tr>
<th>Module Name</th>
<th>Description</th>
<th>Number of Sessions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orientation</td>
<td>Overview of IRT program addressing treatment expectations, descriptions of all modules, and teaching and practice of breathing retraining for anxiety reduction</td>
<td>1-2</td>
</tr>
<tr>
<td>Assessment/Goal Setting</td>
<td>Evaluation and discussion of clients’ character strengths, areas of life satisfaction and dissatisfaction in order to create specific, short, and long-term personally meaningful goals</td>
<td>2-4</td>
</tr>
<tr>
<td>Education about Psychosis</td>
<td>Discussion and discharge about the stress vulnerability model and various aspects of psychosis, including delusional paranoia and delusional mental illness</td>
<td>7-11</td>
</tr>
<tr>
<td>Helplessness Prevention Planning</td>
<td>Discussion of triggers and warning signs, and development of personalized plan for preventing relapse and rehospitalization</td>
<td>2-4</td>
</tr>
<tr>
<td>Processing the Psychotic Episode</td>
<td>Development of cohesive narrative of episode, narrative exposure-based processing of narrative elements, and targeted cognitive restructuring for self-stigmatizing beliefs</td>
<td>5-5</td>
</tr>
<tr>
<td>Developing Resilience</td>
<td>Positive psychology exercises to enhance resilient qualities, increase personal strengths, and build skills around particular strengths in daily life</td>
<td>5-4</td>
</tr>
<tr>
<td>Building a Bridge to Your Goals</td>
<td>Progress and goal review, discussion of possible use of individualized modules with plans for continuation or termination</td>
<td>2-3</td>
</tr>
<tr>
<td>Expected Etiology</td>
<td>Effect on adult’s employment</td>
<td>3-4</td>
</tr>
<tr>
<td>Expected Employment</td>
<td>Effect on adult’s employment</td>
<td>3-4</td>
</tr>
<tr>
<td>Expected Income</td>
<td>Effect on adult’s employment</td>
<td>3-4</td>
</tr>
</tbody>
</table>

**Specialties**

- 7-11 |
- 2-4 |
- 5-5 |
- 5-4 |
- 2-3 |
### Clinician Rating Form

- **Patient endorsed depressed mood on self-report:**
  - You said on the questionnaire that you have been feeling depressed, sad, or down.
  - Tell me about what you have been experiencing. How often did it happen? Does it come and go? How long does it last? How bad is the feeling? (Can you stand it?)

### Clinician Rating Form

- **0 = Not reported**
- **1 = Very Mild:** occasionally feels sad or “down”; of questionable clinical significance
- **2 = Mild:** occasionally feels moderately depressed or often feels sad or “down”
- **3 = Moderate:** occasionally feels very depressed or often feels moderately depressed
Clinician Rating Form

- **4 = Moderately Severe:** often feels very depressed
- **5 = Severe:** feels very depressed most of the time
- **6 = Very Severe:** constant extremely painful feelings of depression
- **☐ Unable to assess (e.g. subject uncooperative or incoherent)**

Navigate First Line Antipsychotics:
- Aripiprazole
- Risperidone
- Quetiapine
- Ziprasidone

Recommended medications for side effect management are:

- **Progression to second medication due to problems with increased weight/metabolic side effects:** Consider switching to aripiprazole or ziprasidone
- **Progression to second medication due to problems with Parkinsonism:** Consider switching to aripiprazole or ziprasidone
- **Progression to second medication due to problems with akathisia:** Consider switching to aripiprazole, risperidone, or ziprasidone
- **Progression to second medication due to problems with adherence:** Consider switching to the long-acting injectable formulation of risperidone, due to its long-acting formulations and availability. Paliperidone is closely related to risperidone and the long-acting version has advantages for monthly administration over the long-acting formulation of risperidone. However, paliperidone palmitate has not been studied with first-episode patients so drawbacks include for first-episode patients. Long-acting injectableolanzapine also has not been studied with first-episode patients. It has a warning for a Post-irrigation Delirium/Seizure Syndrome (POSS) and should only be administered in specialty settings that can provide at least 5 hours of supervision after each injection.
- **Progression to second medication due to problems related to hyperprolactinemia:** Consider switching to aripiprazole, quetiapine, or ziprasidone (note: for patients doing well on first generation agents or risperidone, also consider addition of aripiprazole to their ongoing regimens).
TAU

- Warm hand-off and engagement
- Frequency of appointments
- Use of FEP recommended medications
- Participation in psychosocial interventions
Early Intervention Long Term Results

  - “An interesting research question then arises: if the ‘grip’ is the relaxed, will the individual deteriorate to another plateau or, conversely, will the individual require relatively little maintenance?”
  - Disease Management Modality vs “Altering the course”

Schizophr Bull. 2015 May; 41(3): 617–626.
BMJ. 2017; 356: i6681.

DUP is defined as the time period between onset of psychosis and the onset of criteria treatment. The definition of these time points is as follows:

Onset of psychosis:
(i) one positive rated as moderate or above (4 or above) on PANSS,
(ii) a cluster of positive symptoms reaching a total rating of 7 or more (not rating absent symptoms)

Onset of criteria treatment: the date when adequate treatment commenced which was:
(i) adhering to dosage levels recommended by British the guidelines, and either,
(ii) continued for a period of at least 1 month or
(iii) response

Max Birchwood BiPsych 2013
10-Year Follow-Up of the TIPS Early Detection Psychosis Study:

- Predictive factors of poor outcome:
  - NO association between poor outcome and
    - Premorbid function
    - Gender/age
  - Poor outcome associated with:
    - DUP (DUP 0-1196 weeks)
    - Higher levels of positive symptoms at baseline
    - Duration of positive symptoms in first two years

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**DUP**

- LEO: Mean 10.5mo (17.2)
- OPUS: Mean 126w (187.7) – Median 46w
- STEP: Mean 10mo (15)
- PEPP: Mean 80.9w (118.7) – Median 30.2w
- RAISE: Mean 193.5w (262.2) – Median 74w
- EPPIC: Mean 186d (416.3) – Median 45.9d
- TIPS-ED: Median 5 w – Range 0-1196w

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**4.** Early detection compared with usual detection odds ratio = 2.5, 95% CI = 1.2-5.4, p = 0.017.

**5.** Early detection compared with usual detection odds ratio = 0.5, 95% CI = 0.2-1.2, p = 0.045 (corrected p = 0.017).

**6.** Early detection compared with usual detection odds ratio = 3.1, 95% CI = 1.3-7.3, p = 0.007 (corrected p = 0.017).

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### Table 2. Bonferroni Corrected Pearson Correlations Between Remission, Cognitive Domains, and Functioning at 1 and 2 Years

<table>
<thead>
<tr>
<th>Variable</th>
<th>Functional Outcome at Year 1</th>
<th>Functional Outcome at Year 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remission</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Months in total symptom remission</td>
<td>0.553 (.001*)</td>
<td>-0.037 (.434)</td>
</tr>
<tr>
<td>Months in positive symptom remission</td>
<td>0.283 (.001*)</td>
<td>-0.008 (.910)</td>
</tr>
<tr>
<td>Cognition</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Verbal memory</td>
<td>0.101 (.014)</td>
<td>0.191 (.041)</td>
</tr>
<tr>
<td>Processing speed</td>
<td>0.055 (.129)</td>
<td>0.173 (.056)</td>
</tr>
<tr>
<td>Working memory</td>
<td>0.131 (.088)</td>
<td>0.177 (.056)</td>
</tr>
<tr>
<td>Attention</td>
<td>0.071 (.168)</td>
<td>0.081 (.236)</td>
</tr>
<tr>
<td>Problem-solving</td>
<td>0.101 (.070)</td>
<td>0.453 (.001)</td>
</tr>
<tr>
<td>Visual memory</td>
<td>0.153 (.092)</td>
<td>0.443 (.001)</td>
</tr>
<tr>
<td>Global cognition</td>
<td>0.165 (.032)</td>
<td>0.177 (.056)</td>
</tr>
</tbody>
</table>

*p = <0.001.

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**Arch Gen Psychiatry. 2005;62(9):975-983. doi:10.1001/archpsyc.62.9.975**

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The psychiatrist sees too many end states and deals professionally with too few of the pre-psychotic’ Sullivan, 1927

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At baseline, over one-half (51.7%) of the participants met criteria for a lifetime SUD, including over one-third with alcohol use disorder (36.4%) and with cannabis use disorder (34.7%). Contrary to our hypothesis, there was no treatment group by time interaction effect on days of self-reported substance use over the two-year follow-up.