Early Intervention in Psychotic Disorders: Necessary, Effective, and Overdue

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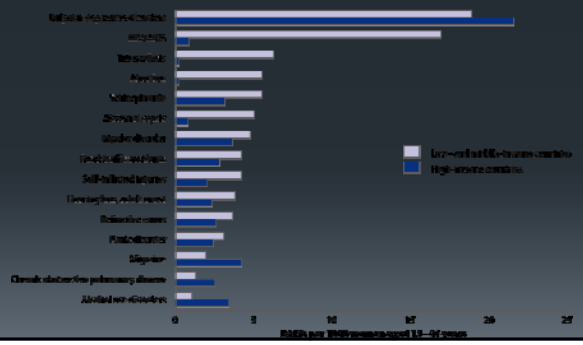
Early intervention in Psychiatric Disorders: Necessary for Population-based Healthcare

- Burden of illness – Disability, Premature mortality
- Healthcare resources
- Societal costs

Psychosis
A final common pathway

- Multiple etiologies:
  - Medical illnesses
  - Drug effects
  - Psychiatric disorders:
    - Schizophrenia
    - Major Depressive Disorder with Psychosis
    - Bipolar Disorder – Mania with Psychosis
    - Schizoaffective Disorder

World Health Organization
Leading causes of disease burden
Women aged 15–44 years, 2004



Poor outcomes and high costs:
Bipolar Disorder

- Recurrent in 90%. Over 50% recur in 1 year
- Avg 5 hospitalizations in 10 years
- 47% of life ill. Days depressed 3X > Days manic
- High suicide rate
- Indirect costs – Disability, premature death
- Lifetime cost for severe cases - $624,785.
- Annual US direct healthcare costs: $45.2 Billion
- Intangible costs
  - Family burden of illness, lost work productivity
  - Impaired Health Related Quality of Life (HRQoL)

Poor outcomes and high costs:
Major Depressive Disorder

- World Health Organization – Global Burden of Disease (1990, 2004 Update)
  - 2nd leading cause of disease burden overall (DALYs)
  - Women 15-44 – Leading cause of disease burden
- Recurrence in 2/3.
- Earlier onset = more recurrence
- Bipolar outcome in many with early onset
- Annual US costs - $83 Billion (2000)

Poor outcomes and high costs:
Schizophrenia

- Continuously or episodically ill – 61%
- Relapse within 1 year – 15-30%
- Suicide in 10%
- Earlier mortality –25 yrs shorter lives
- Annual US costs – $62.7 billion
  - $22.7 Billion – Direct health care

- Most mental illness begins early in life
  - 50% before 14
  - 75% before 25
- Major Depressive Disorder
  - Frequent onset in adolescence.
- Bipolar I Disorder
  - 50-67% onset before age 18. Usually with depression.
- Schizophrenia
  - Neurocognitive deficits in childhood
  - First psychosis between 16 and 25 in 75%

Identifiable patterns of progression. Targets for early treatment

- Non-specific increased risk states
  - MDD - e.g. offspring at risk, adverse or traumatic experience
  - Bipolar – offspring, anxiety, depression
  - Schizophrenia – offspring, neurocognitive deficits
- High Risk states
  - MDD – e.g. Dysthymia + family history mood disorder
  - Bipolar – Major Depression + family history, psychotic subtype, abrupt onset, agitation with antidepressants.
  - Schizophrenia – Attenuated positive symptoms, genetic risk and deterioration, brief limited intermittent psychotic episode
- Early-onset illness

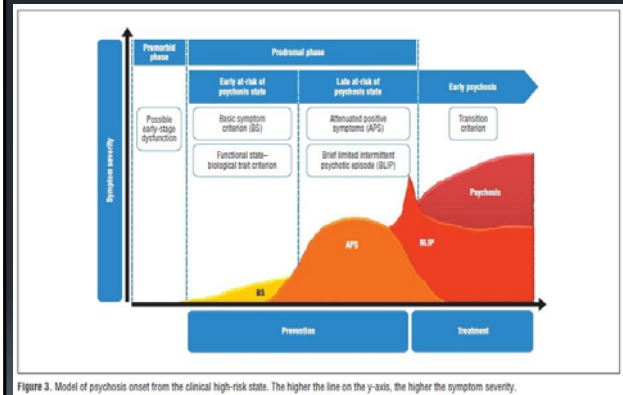


Figure 3. Model of psychosis onset from the clinical high-risk state. The higher the line on the y-axis, the higher the symptom severity.

- Fusar-Poli, et.al, 2013

Earlier treatment and improved outcome:

- Psychosocial effects
  - Maintains family and community support
  - Educational, vocational skill development
  - Preservation of positive sense of self
  - Decrease in adverse experience, trauma (ACEs)
- Neurobiological mechanisms
  - Minimize Neurotoxic effects of decompensated states
    - Glucocorticoid effects
    - Inflammatory processes
- Neuroprotective effects of some agents
  - Lithium, SSRI antidepressants, Omega 3 fatty acids

Early intervention
Major Depressive Disorder

- Early treatment of adolescent depression
  - Decreased substance abuse, educ/voc. Impairment.
  - Decreased suicide attempts, duration of episodes
- Treatment of depression in high-risk adolescents
  - Prevention of Depression Study – Garber J, et.al.,2009
  - High-Risk =
    - Offspring of Depressed adult – And
    - History of depression or current sub-syndromal depression or both.
  - Group CBT effective
    - *Family factor – No effect w actively depressed parent
  - Cost effective.
    - Cost per Quality Adjusted Life Year (QALY) $10-35,000 – lower than medical treatments considered cost-effective. (cf. Lynch FL)

Early Intervention
Bipolar Disorder

- Untreated depression and mania may increase frequency and severity of later episodes
  - Sensitization or Kindling. Post RM, et.al., 1996, 2013
- Early intervention may delay or attenuate progression to a first manic episode
  - Correll CU et.al. – studies underway, unpublished protocol
  - Conus P, et.al, 2008
- Family Focused Therapy decreases frequency and severity of Depressed phase. - Miklowitz D, 2012
  - Increased overall function.
  - Indicated and Secondary Prevention

Early Intervention
Schizophrenia

- Longer untreated psychosis – poor prognosis
  - Wyatt RJ. 1991, Loebel AD, et.al., 1992
- Psychosis High-Risk State – Miller TJ, et.al, 2003.
  - Sub-threshold positive symptoms of psychosis
  - Brief limited intermittent psychotic episodes
  - First-degree relative w psychosis or schizotypal PD plus functional deterioration

:

- 8% - 40% Transition to psychosis in 1 year
  - i.e. 60% to 92% do not develop psychosis in 1 yr

Meta-analysis: Interventions in the High-Risk state – 7 RCTs - Fusar-Poli, et.al., 2013

- Transition to psychosis at 1 year :
  - 23% of controls
  - 7.6% with focused treatment
    - Risk Ratio = 0.34, NNT=6 P<0.001

Antipsychotic medication	NS
Cogn.-Behav. Therapy, Cogn. Therapy (2 trials)	NS
CBT + Antipsychotic medication (2 trials)	NS
Omega 3 Fatty Acids	P 0.02
CBT, Family Psychoeducation, Soc. Skills	P 0.02

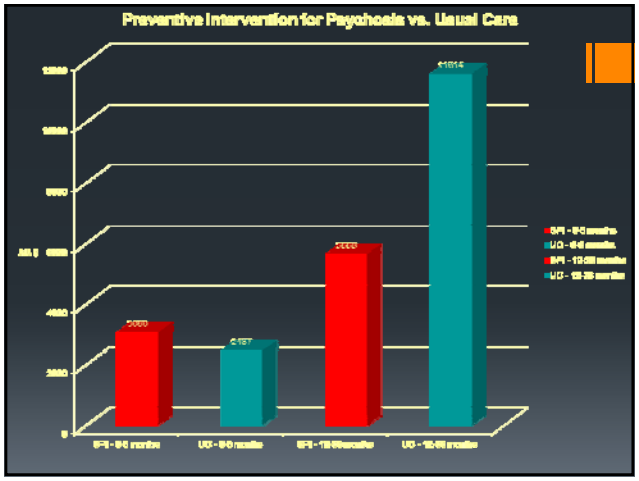
Interventions in the Psychosis High-Risk State - Summary

- Overall – Focused interventions decreased transition to psychosis in 1 year.
- Greatest effect with Omega 3 Fatty Acids
- Significant Adverse Effects with medications
- Recommendation:
  Use safest treatments :
  Psychosocial treatments and Omega-3 Fatty Acids
  Antipsychotic medications only when needed

Costs studies of early intervention psychosis

- Higher Initial Treatment Costs
  - Treatment Phase (6 mo)
    Control – treatment as usual — Total costs = 2,487
    Specific Intervention — Total costs =3.087
- Lower costs, less service use, in 2 yr follow-up
  - Follow-up -12-36 months
    Control — Total costs = 11,614
    Specific Intervention — Total costs = 5,668

Phillips LJ, et.al., 2009 (PACE Clinic, AU)



Intervention in the state of high risk for psychosis

- Family support and psychoeducation
  - PIER Multifamily Psychoeducation Group
- Individual psychotherapy
- Vocational and Educational Support
- Care Coordination
- Team-Based treatment
- Medication as needed for specific impairing symptoms
  - Depression, anxiety, psychotic symptoms
- Health and Wellness
  - Exercise, Diet, Sleep, Screen time, Omega 3 Fatty Acids, Vitamin D

Intervention in First Episode Psychosis

- NIMH – Recovery After Initial Schizophrenia Episode (RAISE)
- Team-Based Treatment vs. Fragmented care
- Care Coordination
- Psychotherapy – Cognitive Behavioral Therapy for Psychosis
- Family Psychoeducation and Support
- Vocational and Educational Support
- Evidence-based Psychopharmacological Treatment

Engagement – Adolescents and Young Adults

- Families
- Peer support
- Identifying patient's needs, priorities
  - Friends
  - School and jobs
  - Physical well-being

Psychopharmacology in early psychosis

- Balance – Effectiveness vs. Adverse Effects
- First meds – Minimal sedation, Extrapyramidal effects
  - Aripiprazole
  - More acute – Risperidone
- Dose ranges - Start low if possible
- Long-Acting Injectable Antipsychotic medications. E.g.
  - Paliperidone Invega Sustenna
  - Risperidone Long-Acting
- Associated symptoms important to the patient:
  - Mood Symptoms
  - Anxiety
  - Insomnia
- Active management of Adverse Effects
  - EPS, Akithesia, Sedation, Weight gain, Sexual

Early intervention for Psychotic Disorders in Maine

- Portland Identification and Early Referral (PIER)
  Focused on Clinical High Risk for Psychosis
  William McFarlane, MD
- Now Is The Time: Healthy Transitions (NITT-HT) – SAMHSA
  - 5 Year grant to Maine DHHS. 2015-2020
  - CHR and First Episode Psychosis, Ages 16-25
  - 25 patients per year. 2 year duration of treatment
  - Initially Cumberland County. Expansion to Androscoggin, York, Penobscot
  - Maine Medical Center, Youth Move, Transition to Independence (TIP)

NITT-HT: Year One

- Year One, Month 10: 27 patients
- Diagnoses – first 25:

Clinical High Risk for Psychosis	1
Schizophrenia	7
Major Depressive Disorder w Psychosis	5
Bipolar Disorder – Mania w Psychosis	4
Schizophrenia Spectrum – Other	6
Schizoaffective Disorder	2

NITT-HT: Year One Functional outcomes

- World Health Organization Disability Assessment Scale (WHODAS)

Diagnosis	Intake	90 days	180	270
Schizophrenia				
Maj Depr w P				
Bipolar M w P				
Psychosis Other				
SchizoAffective				

Opportunities – Clinical Studies

- Identification of predictors of maladaptive family interaction, before it develops
- Medical morbidity is low in early stages. Aggressive prevention of obesity, metabolic syndrome
- Substance abuse in many is not yet begun or firmly established. Active focus on protective factors
- Early indicators of physiological CNS stress. Cortisol dysregulation and inflammatory cytokines