Preventing Psychotic Disorders by Early Detection and Intervention

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Early detection and prevention in another illness

“If you catch cancer at Stage 1 or 2, almost everybody lives. If you catch it at Stage 3 or 4, almost everybody dies.

We know from cervical cancer that by screening you can reduce cancer up to 70 percent. We’re just not spending enough of our resources working to find markers for early detection.”

Lee Hartwell, MD
Nobel Laureate, Medicine
President and Director,
Hutchinson Center
New York Times Magazine
December 4, 2005, p. 56
Early detection and prevention in psychotic illness

“The psychiatrist sees too many end states and deals professionally with too few of the pre-psychotic.”

—Harry Stack Sullivan, 1927

75%
Proportion of people who have their first psychotic episode before age 25.

2-3%
Proportion of youth who develop schizophrenia or a severe, psychotic mood disorder
25

Years of life lost by people with schizophrenia due to all causes, including heart disease, cancer and suicide

>33 : 1

Odds that a person with or without psychotic symptoms will attempt or commit suicide

After: Cornblatt, et al., 2005
Early prodrome

Illusions
Dread
Insomnia
Anorexia
Social deficits
Social & performance deficits
Perceptual distortions
Pervasive anxiety
Withdrawal
“Oddness”
Functional deterioration

Late prodrome

Critical comments
CD, EOI
Anxiety
Path: Manifestation
High EE

Acute onset

Psychosis

Biosocial causal interactions in late schizophrenic prodrome

Is early intervention indicated prevention of psychotic disorders?

“Yes, we can.”

Risk of psychosis over 10 years
Trials of Indicated Prevention

- Buckingham, UK
- OPUS, Denmark
- PIER, Maine
- EDIPPPP, USA
- GRN
- PACE I, II, Australia
- EDIE I, II, III, UK
- Addington, Canada
- PRIME, North America
- Omega-3 FAs, Austria

Family psychoeducation
Cognitive therapy
Biological treatment

Early intervention is prevention

One year rates for conversion to psychosis
Risk reduction = 66%

Meta-analyses of RCTs
Conversion to psychosis

<table>
<thead>
<tr>
<th>Study</th>
<th>Risk ratio (risk reduction)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fusar-Poli, et al, 2013</td>
<td>0.34 (-66%; n=554)</td>
</tr>
<tr>
<td>van der Gaag, et al, 2013</td>
<td>0.46 (-54%)</td>
</tr>
<tr>
<td>Stafford, et al, 2013</td>
<td>0.54 (-46%; n=1246)</td>
</tr>
<tr>
<td>Integrated treatment</td>
<td>0.19 (-81%)</td>
</tr>
<tr>
<td>(Nordentoft, 2006; Bechdolf, 2013)</td>
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</table>
Portland Identification and Early Referral (PIER)

Reducing the incidence of major psychotic disorders in a defined population, by early detection and treatment:
Indicated prevention
Ages 12-35

Professional and Public Education

- Reducing stigma
- Information about modern concepts of psychotic disorders
- Increasing understanding of early stages of mental illness and prodromal symptoms
- How to get consultation, specialized assessments and treatment quickly
- Ongoing inter-professional collaboration

PIER Team

- Family practitioners
- Pediatricians
- School teachers, guidance counselors, nurses, social workers, Employers
- College health services
- Mental health clinicians
- Military bases and recruiters
- Clergy
- Advertising
- Emergency and crisis services
- General Public

PIER Team

Employers
Assessing Risk for Psychosis

Signs of prodromal psychosis
Schedule of Prodromal Syndrome (SOPS), McGlashan, et al

A clustering of the following:
Changes in behavior, thoughts and emotions, with preservation of insight, such as:
- Heightened perceptual sensitivity
- Magical thinking
  - Demiunification, depersonalization, grandiose ideas, child-like logic
  - Unusual perceptual experiences
  - "Presence", imaginary friends, fleeting apparitions, odd sounds
- Unusual fears
  - Avoidance of bodily harm, fear of assault (cf. social phobia)
- Disorganized or deranged thought
  - Receptive and expressive aphasia
  - Uncharacteristic, peculiar behavior
  - Satanic preoccupations, unpredictable, bizarre appearance
- Reduced emotional or social responsiveness
  - "Depression", agitation, amnesia, mild dementia
Signs of prodromal psychosis

- 2. Significant deterioration in functioning
  - Unexplained decrease in work or school performance
  - Decreased concentration and motivation
  - Decrease in personal hygiene
  - Decrease in the ability to cope with life events and stressors

- 3. Social withdrawal
  - Loss of interest in friends, extracurricular sports/hobbies
  - Increasing sense of disconnection, alienation
  - Family alienation, resentment, increasing hostility, paranoia

Intervening to Prevent Onset

Family-aided Assertive Community Treatment (FACT):
Clinical and functional intervention

- Rapid, crisis-oriented initiation of treatment
- Psychosocially multifamily groups
- Case management using key Assertive Community Treatment methods
  - Integrated, multidisciplinary team; outreach PRN; rapid response; continuous case review
- Supported employment and education
- Collaboration with schools, colleges and employers
- Cognitive assessments used in school or job
- Low-dose atypical antipsychotic medication
  - 5-20 mg aripiprazole, 2.5–7.5 mg olanzapine, 0.25-3 mg risperidone
- Mood stabilizers, as indicated by symptoms:
  - SSRI, with caution, especially with aripiprazole and/or a family history of manic episodes
  - Mood stabilizing drugs: lamotrigine 50–150 mg, valproic acid, 500–1500 mg, lithium at therapeutic doses by blood level, 0.6-1.0
Components of first episode psychosis services:
Evidence level A and rated as essential by international experts

<table>
<thead>
<tr>
<th>Components with level of supporting evidence (A-D)</th>
<th>Rating (Semi-Interquartile; maximum = 0.5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Selection of Antipsychotic Medication (Level of evidence: A)</td>
<td>.5</td>
</tr>
<tr>
<td>Clozapine for Treatment-Resistance (Level of evidence: A)</td>
<td>.5</td>
</tr>
<tr>
<td>Use of Single Antipsychotics (Level of evidence: A)</td>
<td>.5</td>
</tr>
<tr>
<td>Psychoeducational Multifamily Group (Level of evidence: A)</td>
<td>.5</td>
</tr>
<tr>
<td>Supported Employment (Level of evidence: A)</td>
<td>.37</td>
</tr>
</tbody>
</table>


Key clinical strategies in family intervention specific to prodromal psychosis

• Strengthening relationships and creating an optimal, protective home environment:
  – Reducing intensity, anxiety and over-involvement
  – Preventing onset of negativity and criticism
  – Adjusting expectations and performance demands
  – Minimizing internal family stressors
    • Marital stress
    • Sibling hostility
    • Conflict and disagreement
  – Buffering external stressors
    • Academic and employment stress
    • Social rejection at school or work
    • Cultural taboos
    • Entertainment stress
    • Romantic and sexual complications

Relapse Outcomes in Clinical Trials with Schizophrenia
Stages of a Psychoeducational Multifamily Group

- Joining
  - Families and clients; 1 – 2 years
  - Problem-solving & Networking

- Educational Workshop
  - Families and clients; 4 – 6 hours with focus on Family Guidelines

- Ongoing MFG
  - Families and clients; 1 – 2 years
  - Problem-solving & Networking

Social networks in schizophrenia

- Family network size
  - diminishes with length of illness
  - decreases in the period immediately following a first episode
  - is smaller at the time of first admission

- Networks
  - buffer stress and adverse events
  - determine treatment compliance
  - predict relapse rate
  - correlate with coping skills and burden.

Outcomes
Referral sources

<table>
<thead>
<tr>
<th>Source</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family</td>
<td>185</td>
<td>23.7</td>
</tr>
<tr>
<td>Educational professionals</td>
<td>158</td>
<td>20.3</td>
</tr>
<tr>
<td>Mental health agencies</td>
<td>204</td>
<td>26.2</td>
</tr>
<tr>
<td>Tertiary hospitals, ERs</td>
<td>168</td>
<td>21.5</td>
</tr>
<tr>
<td>Community physicians, therapists</td>
<td>38</td>
<td>4.9</td>
</tr>
<tr>
<td>Self and other</td>
<td>10</td>
<td>1.3</td>
</tr>
</tbody>
</table>

Treated cases converting to psychosis within 24 months (n = 148)

- Cases not converted 121 81.8%
- Cases converted, 1-30 days 14 9.4%
- SOPS psychosis conversions 13 8.8%

First hospitalizations for psychosis
Maine Urban controls areas vs. Greater Portland

*p<0.0001
PIER long-term outcome
4-12 years after identification of risk

During 2-year treatment, 2001-2009

Received any treatment 139 100%
Severe episode 14 10%

Post-2-year treatment, 2-10 years

Followed-up 72 52%
Severe psychosis or hospitalization 9 13%
In school or working 55 76%

Early Detection and Intervention for the Prevention of Psychosis

• Effectiveness Trial at six sites:
  – Portland, Maine / Maine Medical Center
  – Glen Oaks, New York / Albert Einstein College of Medicine
  – Ann Arbor, Michigan / University of Michigan
  – Salem, Oregon / Oregon Health Sciences University
  – Sacramento, California / University of California at Davis
  – Albuquerque, New Mexico / University of New Mexico

• Sponsored by RWJF
• Risk-based allocation and incidence reduction
• Regression discontinuity and time series analyses
• Large and diverse nationally representative sample
• PIER community outreach and identification systems

Entry and assignment criteria

• Ages 12-25
• Living in the experimental catchment area
• Positive symptom score by SIPS/SOPS criteria:
  – Clinical Low Risk (CLR) Control
    • Sum <7; OR
  – Clinical High-Risk (CHR) Treatment
    • Sum = 7 or more; OR
  – Early First Episode Psychosis (EFEP) Treatment
    • Any 6 for < 1 month
• IQ 70 or higher
• No previous psychosis
• Not toxic or medical psychosis
Outcomes

Early identification across sites

<table>
<thead>
<tr>
<th>SITE</th>
<th>Population</th>
<th>Age-corrected rate**</th>
<th>Years of community outreach</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maine</td>
<td>323,185</td>
<td>63%</td>
<td>8</td>
</tr>
<tr>
<td>Michigan</td>
<td>344,791</td>
<td>37%</td>
<td></td>
</tr>
<tr>
<td>Oregon</td>
<td>631,853</td>
<td>29%</td>
<td>2.5</td>
</tr>
<tr>
<td>California</td>
<td>466,488</td>
<td>26%</td>
<td></td>
</tr>
<tr>
<td>New York</td>
<td>587,725</td>
<td>17%</td>
<td>1.5</td>
</tr>
<tr>
<td>New Mexico</td>
<td>662,564</td>
<td>12%</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>2,986,526</td>
<td>27%</td>
<td></td>
</tr>
</tbody>
</table>

** Proportion (69.2%) of ages 12-35 population represented by ages 12-25 population

*Rate for Nottingham, U.K., in Kirkbride, et al., Arch Gen Psychiatry. 2006;63:250-258

Number of outreach activities and referrals within catchment areas during two years, by town or by zip code

- Michigan
- One dot = one event Year 2 (3/09-3/10)
- Catchment Area Outreach Activities
- Referrals

(Images of maps showing outreach activities and referrals)
### Demographic and Psychosocial Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Total (n = 337)</th>
<th>Clinical Low-Risk (n = 87)</th>
<th>Treatment High-Risk (n = 250)</th>
<th>Clinical High-Risk (n = 205)</th>
<th>Early 1st Episode (n = 45)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean)</td>
<td>16.4</td>
<td>16.2</td>
<td>16.4</td>
<td>17.9</td>
<td></td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>134 (40%)</td>
<td>26 (30%)</td>
<td>89 (35%)</td>
<td>19 (42%)</td>
<td></td>
</tr>
<tr>
<td>Caucasian, %</td>
<td>62%</td>
<td>71%</td>
<td>61%</td>
<td>47%</td>
<td></td>
</tr>
<tr>
<td>African-American, (%)</td>
<td>9%</td>
<td>6%</td>
<td>8%</td>
<td>22%</td>
<td></td>
</tr>
<tr>
<td>Asian-American, n (%)</td>
<td>13 (4%)</td>
<td>0 (0%)</td>
<td>9 (4%)</td>
<td>8 (7%)</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>15%</td>
<td>9 (9%)</td>
<td>33 (17%)</td>
<td>6 (16%)</td>
<td></td>
</tr>
<tr>
<td>In School/Working, %</td>
<td>83%</td>
<td>84%</td>
<td>84%</td>
<td>80%</td>
<td></td>
</tr>
<tr>
<td>Income (dollars)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>40K – 50K</td>
<td>50K – 60K</td>
<td>40K – 50K</td>
<td>50K – 60K</td>
<td></td>
</tr>
</tbody>
</table>

### Clinical Characteristics

<table>
<thead>
<tr>
<th>Current SCID-IV Axis-I Diagnoses</th>
<th>Total (n = 337)</th>
<th>Clinical Low-Risk (n = 87)</th>
<th>Treatment High-Risk (n = 250)</th>
<th>Clinical High-Risk (n = 205)</th>
<th>Early First Episode (n = 45)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Diagnosis</td>
<td>14%</td>
<td>22%</td>
<td>14%</td>
<td>8%</td>
<td>.01</td>
<td></td>
</tr>
<tr>
<td>Mood Disorder</td>
<td>42%</td>
<td>37%</td>
<td>49%</td>
<td>18%</td>
<td>.01</td>
<td></td>
</tr>
<tr>
<td>(1) Bipolar</td>
<td>16 (5%)</td>
<td>2 (2%)</td>
<td>12 (6%)</td>
<td>3 (15%)</td>
<td>.38</td>
<td></td>
</tr>
<tr>
<td>(2) Major Depression</td>
<td>114 (34%)</td>
<td>27 (31%)</td>
<td>83 (41%)</td>
<td>3 (16%)</td>
<td>.38</td>
<td></td>
</tr>
<tr>
<td>Substance Abuse</td>
<td>28 (8%)</td>
<td>8 (9%)</td>
<td>7%</td>
<td>5 (11%)</td>
<td>.46</td>
<td></td>
</tr>
</tbody>
</table>

### Rates of Conversion or Relapse

**Over 24 months**

<table>
<thead>
<tr>
<th></th>
<th>CLR</th>
<th>CHR</th>
<th>EFEP</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>87</td>
<td>205</td>
<td>45</td>
</tr>
<tr>
<td>Severe Psychosis</td>
<td>2.3%</td>
<td>6.3%</td>
<td></td>
</tr>
<tr>
<td>Relapse</td>
<td></td>
<td></td>
<td>11%</td>
</tr>
<tr>
<td>Negative Events*</td>
<td>22%</td>
<td>25%</td>
<td>40%</td>
</tr>
</tbody>
</table>

*Hospitalizations, incarcerations, suicide attempts, assaults, rape
Psychotic Symptoms

Baseline 6 Months 12 months 24 months

 Controls APS EFEP

CHR vs. CLR = 0.0034
EFEP vs. CLR <0.0001

Negative Symptoms

Baseline 6 Months 12 months 24 months

 Controls APS EFEP

CHR vs. CLR = 0.099
EFEP vs. CLR <0.012

Global Test: Treatment vs. Control
Overall outcomes over 24 months across ten clinical and functional variables

Clinical High Risk Subsample
Estimate  S.E.  t  p
0.38    0.17  2.26  0.0244

EFEP Subsample  t  p
1.05    0.28  3.77  0.0002

Both Treatment Subsamples  t  p
7.50    0.0007
In school or working:
Baseline and 24 months

Increases in participation in school, work or work
and school from baseline to 24 months*

Hospital Admissions for First Episode Psychosis
Intervention areas / control areas: CA, ME, MI, NY, OR

* Odds Ratio, CHR+EFEP vs. CLR, = 3.44, 95% C.I. 1.16, 11.0, p=0.025
Outcomes in Four California PIER Programs*

<table>
<thead>
<tr>
<th>N = 125 Baseline</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Working</td>
<td>15%</td>
</tr>
<tr>
<td>In school</td>
<td>57%</td>
</tr>
<tr>
<td>Onset of Psychosis:</td>
<td>21%</td>
</tr>
<tr>
<td>Hospitalizations:</td>
<td>13%</td>
</tr>
<tr>
<td>Suicide attempts:</td>
<td>8%</td>
</tr>
</tbody>
</table>

*San Diego, Santa Clara (San Jose), Ventura Counties

Conclusions

- Community-wide education is feasible.
- Referral of 30% up to 60% of the at-risk population.
- Global outcome in FACT was better than regular treatment.
- The rate of psychosis onset is less than 1/4 of expected.
- Average functioning was in the normal range by 24 months.
- Five cities show a declining incidence.
- Programs in California are showing same results.
- ¾ were in school or working up to 10 years later.
For further information:

www.piertraining.org

PTI@maine.rr.com