Now Is the Time

Preventing Psychotic Disorders by Early Detection and Intervention

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“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
Cognitive Deficits

Affective Sx: Depression

Social Isolation

School Failure

Biological Vulnerability: CASIS

Early Insults

e.g. Disease
Genes, Possibly
Viral Infections,
Environmental
Toxins

Brain Abnormalities

Structural
Biochemical
Functional

Social and Environmental Triggers

Increasing Positive symptoms

After Comblatt, et al., 2005
Is early intervention indicated prevention of psychotic disorders?

“Yes, we can.”
Risk of psychosis over 10 years

% of at-risk subjects converting to psychosis
Trials of Indicated Prevention

- Buckingham, UK
- OPUS, Denmark
- PIER, Maine
- EDIPPP, 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%

Fusar-Poli, et al, JAMA Psychiatry, 2013
## 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 (Nordentoft, 2006; Bechdolf, 2012)</td>
<td>• 0.19 (-81%)</td>
</tr>
</tbody>
</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
Family practitioners

Pediatricians

School teachers, guidance counselors, nurses, social workers
Employers

College health services

Mental health clinicians

Military bases and recruiters

Clergy

Emergency and crisis services

Advertising

General Public

PIER Team

The PIER Program
"an ounce of prevention"
Family practitioners

Pediatricians

School guidance counselors, nurses, social workers

Employers

College health services

Mental health clinicians

Military bases and recruiters

Clergy

Emergency and crisis services

General Public

PIER Team
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
  - To light, noise, touch, interpersonal distance
- Magical thinking
  - Derealization, 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 digressive speech*
  - Receptive and expressive aphasia
- Uncharacteristic, peculiar behavior
  - Satanic preoccupations, unpredictability, bizarre appearance
- Reduced emotional or social responsiveness
  - "Depression", alogia, anergia, 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
- Psychoeducational 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:
  - SSRIs, with caution, especially with aripiprazole and/or a family history of manic episodes
  - Mood stabilizing drugs: lamotrigine 50-150 mg, valproate, 500-1500mg, 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
    - Confusion 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

- No medication: 65
- Individual therapy & medication: 41
- FPE & medication: 15
- PEMFG & medication: 9
Stages of a Psychoeducational Multifamily Group

Joining
- Family and client separately + together;
- 3 - 6 weeks;
- Start psychoeducation

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>Count</th>
<th>Percentage</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

Historical Control Period 1999-2000
Intervention Period 2001-2007

Urban Control Areas
- +8%
- Net difference = 34%*

Portland Area
- -26%

* p < 0.0001

Historical Control Period 1999-2000
Intervention Period 2001-2007
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**, at 25/100,000*</th>
<th>Years of community outreach</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maine</td>
<td>323,105</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>557,725</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><strong>Total</strong></td>
<td><strong>2,986,526</strong></td>
<td><strong>27%</strong></td>
<td></td>
</tr>
</tbody>
</table>

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

** Proportion (69.2%) of ages 12-35 population represented by ages 12-25 population
Number of outreach activities and referrals within catchment areas during two years, by town or by zip code (3/08-2/09)

- California
- One dot = one event Year 2 (3/09-3/10)
- Catchment Areas Outreach Activities 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>16.6</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 (43%)</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>4 (5%)</td>
<td>9 (4%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>15%</td>
<td>8 (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>40K – 50K</td>
<td>50K – 60K</td>
<td>40K – 50K</td>
<td>30K – 40K</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 (CLR) (n = 87)</th>
<th>Treatment (High-Risk) (n = 250)</th>
<th>Clinical High Risk (CHR) (n = 205)</th>
<th>Early First Episode (EFEP) (n = 45)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Diagnosis</td>
<td>14%</td>
<td>22%</td>
<td>14%</td>
<td>0%</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>&lt;.01</td>
<td></td>
</tr>
<tr>
<td>(1) Bipolar</td>
<td>16 (5%)</td>
<td>2 (2%)</td>
<td>12 (6%)</td>
<td>3 (7%)</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 (7%)</td>
<td>&lt;.01</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>.66</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><strong>n</strong></td>
<td>87</td>
<td>205</td>
<td>45</td>
</tr>
<tr>
<td><strong>Severe</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psychosis</td>
<td>2.3%</td>
<td>6.3%</td>
<td></td>
</tr>
<tr>
<td><strong>Relapse</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>11%</td>
</tr>
<tr>
<td><strong>Negative</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Events*</td>
<td>22%</td>
<td>25%</td>
<td>40%</td>
</tr>
</tbody>
</table>

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

CHR vs. CLR = 0.0034
EFEP vs. CLR <0.0001
Global Test: Treatment vs. Control

Overall outcomes over 24 months across ten clinical and functional variables

Clinical High Risk Subsample

<table>
<thead>
<tr>
<th>Estimate</th>
<th>S.E.</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.38</td>
<td>0.17</td>
<td>2.26</td>
<td>0.0244</td>
</tr>
</tbody>
</table>

EFEP Subsample

<table>
<thead>
<tr>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.77</td>
<td>0.0002</td>
</tr>
</tbody>
</table>

Both Treatment Subsamples

<table>
<thead>
<tr>
<th>f</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.50</td>
<td>0.0007</td>
</tr>
</tbody>
</table>
In school or working:
Baseline and 24 months

- CLR
  - Baseline: 88%
  - 24 months: 79%
- CHR + EFEP
  - Baseline: 84%
  - 24 months: 83%
Increases in participation in school, work or work and school from baseline to 24 months*

<table>
<thead>
<tr>
<th></th>
<th>CLR (n=57)</th>
<th>CHR&amp;EFEP (n=170)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increasing participation</td>
<td>7.0%</td>
<td>20.6%</td>
</tr>
</tbody>
</table>

* Odds Ratio, CHR+EFEP vs. CLR, = 3.44, 95% C.I. 1.16, 11.0, p=0.025
Hospital Admissions for First Episode Psychosis
Intervention areas / control areas: CA, ME, MI, NY, OR

Program starts

- R² = 0.977

Control period  Forecast  Intervention period
# Outcomes in Four California PIER Programs

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Baseline</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Working</td>
<td>15%</td>
<td>49%</td>
</tr>
<tr>
<td>In school</td>
<td>57%</td>
<td>56%</td>
</tr>
<tr>
<td>Onset of Psychosis:</td>
<td>21%</td>
<td>3%</td>
</tr>
<tr>
<td>Hospitalizations:</td>
<td>13%</td>
<td>7%</td>
</tr>
<tr>
<td>Suicide attempts:</td>
<td>8%</td>
<td>2%</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.
The Catcher in the Rye

a novel by J. D. Salinger
For further information:

www.piertraining.org

PTI@maine.rr.com