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
Mental health and substance use disorders account for 60% of the non-fatal burden of disease amongst young people aged 15-34. 

Developed by Patrick McGorry, MD

Cognitive Deficits
Affective Sx: Depression
Social Isolation
School Failure

Biological Vulnerability: CASIS

Brain Abnormalities
Biochemical Functional

Disability

Effects of untreated initial psychosis

• Being psychotic is traumatic and can be stigmatizing.
• Psychosis can reduce cognitive and social functioning.
• The individual may lose contact with family and friends, fail school, or drop out of work/school.
• Without treatment, neurobiological deficits that underlie symptoms can progress.
• The longer the psychosis lasts, the more difficult it may be for the therapist to establish a good therapeutic relationship with the patient.
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
- 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

<table>
<thead>
<tr>
<th>Rate</th>
<th>PACE</th>
<th>PRIME</th>
<th>OPUS</th>
<th>PIER</th>
<th>EDIE</th>
<th>O-3</th>
<th>PACE II</th>
<th>GRN</th>
<th>EDIE II</th>
</tr>
</thead>
<tbody>
<tr>
<td>%</td>
<td>22.9</td>
<td>7.6</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>23.0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Addington

Mean rate

<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=1244)</td>
</tr>
<tr>
<td>Integrated treatment (Nordentoft, 2006; Bechdolf, 2012)</td>
<td>0.19 (-81%)</td>
</tr>
</tbody>
</table>

Fusar-Poli, et al, JAMA Psychiatry, 2013

Risk reduction = 66%

Meta-analyses of RCTs

Conversion to psychosis

Early detection makes a difference

Early intervention is associated with:
- More rapid and complete recovery
- Preservation of brain functioning
- Preservation of psychosocial skills
- Decreased need for intensive treatments
- Preservation of supports, especially family/friends
- Less stigma and perception of rejection
Partnering with families in the early phases of psychosis preserves family connections by increasing understanding, reducing stress and relieving burden.

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

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
Assessing Risk for Psychosis
Psychosis occurs on a spectrum

Youth enjoys basketball and plans to attend college on a full scholarship.

Grandiosity

Youth is heading to New York City because he believes he is talented enough to join the Knicks.

Suspiciousness

Young woman goes to the mall and feels like people are looking at her sometimes.

Auditory hallucinations

Hearing a voice clearly outside one’s head saying, “You’re a loser” or “You’re a failure.”

Early warning signs before psychosis starts

• Feeling “something’s not quite right”
• Having unusual thoughts and confusion
• Experiencing fear for no good reason
• Hearing sounds/voices that are not there
• Declining interest in people, activities and self-care
• Having trouble communicating and understanding

People with emerging psychosis often experience:

• Social withdrawal
• Odd, unusual behaviors
• Decreased motivation
• Inability to enjoy activities
• Mood swings
• Pervasive anxiety
• Disrupted sleep patterns, and
• Changes in appetite and eating
• Preoccupation with physical symptoms
Signs of prodromal psychosis

- Significant deterioration in functioning
  - Unexplained decrease in work or school performance
  - Decrease in personal hygiene
  - Decrease in the ability to cope with life events and stressors
- 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
  - Supported employment and education
  - Collaboration with schools, colleges and employers
  - Cognitive assessments used in school or job
  - Low-dose atypical antipsychotic medication
  - Mood stabilizers, as indicated by symptoms:
Components of first episode psychosis services: Evidence level A and rated as essential by international experts

| Components with level of supporting evidence (A-D) | Rating  
(Semi-Interquartile; maximum = 0.5) |
<table>
<thead>
<tr>
<th></th>
<th></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
  - Buffering external stressors

Relapse Outcomes in Clinical Trials with Schizophrenia

- No medication
- Individual therapy & medication
- FIPs & medication
- FAPs & medication
Stages of a Psychoeducational Multifamily Group

- Joining: Families and clients; 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>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 (81.2%)
- Cases converted, 1-30 days: 14 (9.4%)
- Full psychosis conversions: 14 (9.4%)

First hospitalizations for psychosis

Maine Urban controls areas vs. Greater Portland

<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Urban Areas</td>
<td>Portland Area</td>
</tr>
<tr>
<td>0%</td>
<td>+8%</td>
</tr>
<tr>
<td>5%</td>
<td>-26%</td>
</tr>
<tr>
<td>10%</td>
<td>Net difference = 34%*</td>
</tr>
</tbody>
</table>

* 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
- 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
  - 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>323,015</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>466,400</td>
<td>26%</td>
<td></td>
</tr>
<tr>
<td>New York</td>
<td>887,725</td>
<td>17%</td>
<td>1.5</td>
</tr>
<tr>
<td>New Mexico</td>
<td>662,364</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>

**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

---

### Diagram

- Map of Michigan with catchment areas indicated.
- Legend with dots representing events.
<table>
<thead>
<tr>
<th>Demographic and Psychosocial Characteristics</th>
<th>Clinical Characteristics</th>
<th>Rates of Conversion or Relapse Over 24 months</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total</strong> <em>(n = 337)</em></td>
<td><strong>Clinical</strong> <em>(n = 87)</em></td>
<td><strong>CLR</strong>*(87)* <strong>CHR</strong>*(205)* <strong>EFEP</strong>*(45)*</td>
</tr>
<tr>
<td><strong>Clinical High-Risk</strong> <em>(n = 205)</em></td>
<td></td>
<td><strong>Severe Psychosis</strong> 2.3% 6.3%</td>
</tr>
<tr>
<td><strong>Early 1st Episode</strong> <em>(n = 45)</em></td>
<td></td>
<td><strong>Relapse</strong> 11%</td>
</tr>
<tr>
<td><strong>Age (mean)</strong> 16.6 16.2 16.4 17.9</td>
<td></td>
<td><strong>Negative Events</strong> 22% 25% 40%</td>
</tr>
<tr>
<td><strong>Female, n (%)</strong> 134 (40%) 26 (30%) 89 (43%)</td>
<td></td>
<td><em>Hospitalizations, incarcerations, suicide attempts, assaults, rape</em></td>
</tr>
<tr>
<td><strong>Caucasian, %</strong> 62% 71% 61% 47%</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>African-American, %</strong> 9% 6% 8% 22%</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Asian-American, n (%)</strong> 13 (4%) 4 (5%) 9 (4%) 0 (0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Hispanic</strong> 15% 9% 8% 80%</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Income (dollars)</strong> 0-1, =10K 50K-60K 60K-70K 70K-80K</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Clinical Characteristics</strong></th>
<th><strong>Total</strong> <em>(n = 337)</em></th>
<th><strong>Clinical Low-Risk</strong> <em>(n = 87)</em></th>
<th><strong>Treatment High-Risk</strong> <em>(n = 250)</em></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Current SCID-IV Axis I</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Diagnoses</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>No Diagnosis</strong></td>
<td>14%</td>
<td>22%</td>
<td>14%</td>
</tr>
<tr>
<td><strong>Mood Disorder</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(1) Bipolar</td>
<td>5%</td>
<td>2%</td>
<td>6%</td>
</tr>
<tr>
<td>(2) Major Depression</td>
<td>114 (34%)</td>
<td>27 (31%)</td>
<td>83 (41%)</td>
</tr>
<tr>
<td><strong>Substance Abuse</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Total)</td>
<td>28 (8%)</td>
<td>8 (9%)</td>
<td>205 (11%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Rates of Conversion or Relapse</strong></th>
<th><strong>CLR</strong></th>
<th><strong>CHR</strong></th>
<th><strong>EFEP</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Severe Psychosis</strong></td>
<td>2.3%</td>
<td>6.3%</td>
<td></td>
</tr>
<tr>
<td><strong>Relapse</strong></td>
<td>11%</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Negative Events</strong></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

Negative Symptoms

Baseline 6 Months 12 Months 24 Months

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  f  p
7.50    0.0007
In school or working:
Baseline and 24 months

<table>
<thead>
<tr>
<th></th>
<th>CLR (n=57)</th>
<th>CHR +EFEP (n=170)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>79%</td>
<td>84%</td>
</tr>
<tr>
<td>24 months</td>
<td>88%</td>
<td>83%</td>
</tr>
</tbody>
</table>

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 +EFEP (n=170)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>7.0%</td>
<td>20.6%</td>
</tr>
<tr>
<td></td>
<td>0%</td>
<td>5%</td>
</tr>
<tr>
<td></td>
<td>15%</td>
<td>20%</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

- Control period
- Program starts

R² = 0.97705
Outcomes in Four California PIER Programs*

<table>
<thead>
<tr>
<th></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.
For further information:

www.piertraining.org

PTI@maine.rr.com