Clinical Trials to Prevent Full Onset of Psychosis for Those at Elevated Risk

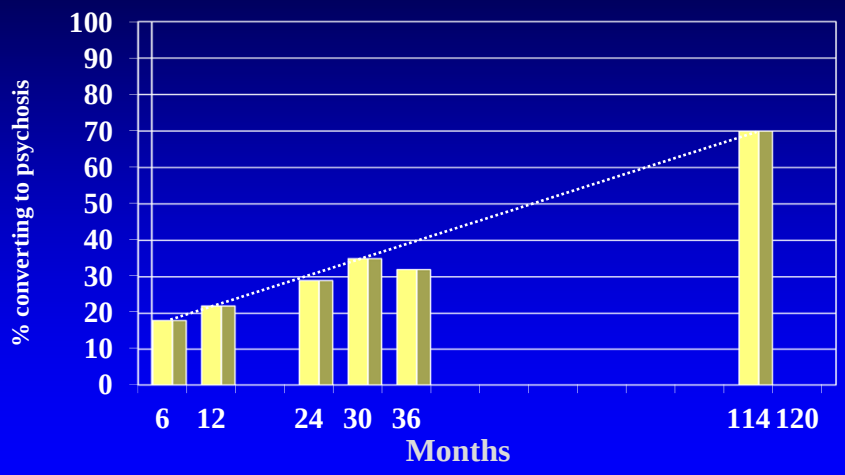
Over the past decade several clinical trials have been conducted, testing a variety of treatments to prevent the onset of full psychosis in those found to be at elevated risk. The first report was by Ian Falloon, working in Buckingham, UK. He noted a large decrease in incidence of schizophrenia in the county four years after he trained general practitioners to identify patients at risk and refer them for family intervention and medication.

There are now 12 trials in the literature and three meta-analyses, illustrated in the images on the following pages. Across time, there has been a consistent trend that those offered family psychoeducation, cognitive behavioral therapy, antipsychotic medication, omega-3 fatty acids or various combinations have had rates of conversion to psychosis averaging about 8%, while the rates in the control conditions have averaged 23%. All three meta-analyses of these studies have concluded that there is a significant benefit from treatment at this stage.

There has been some controversy about the results, but the inconsistency has been in the *control* groups, rather than the experimental treatment groups. The two studies with very low rates in the control groups were in locations in which early identification had been underway for over 15 years, suggesting that those entering more recent studies in those areas were at lower risk, simply because those at higher risk had either already converted or entered previous studies and been prevented. That is suggested by the fact that in Portland, Maine, incidence of hospitalization for first-episode psychosis dropped by 26% after just six years of operation by the PIER program there, as seen in one of the illustrations in the slides that follow.

Risk of psychosis over time

In no-treatment or control samples



PREVENT MENTAL ILLNESS WITH EARLY DETECTION

The PIER Program "an ounce of prevention"

Trials of Indicated Prevention

- Buckingham, UK
- OPUS, Denmark
- PIER, Maine
- EDIPPP, USA
- GRN, Germany
- PACE I, II, Australia
- EDIE I, II, III, UK
- Addington, Canada
- Van der Gaag, Netherlands
- PRIME, North America
- Omega-3 FAs, Austria

Family psychoeducation

Cognitive therapy

Biological treatment

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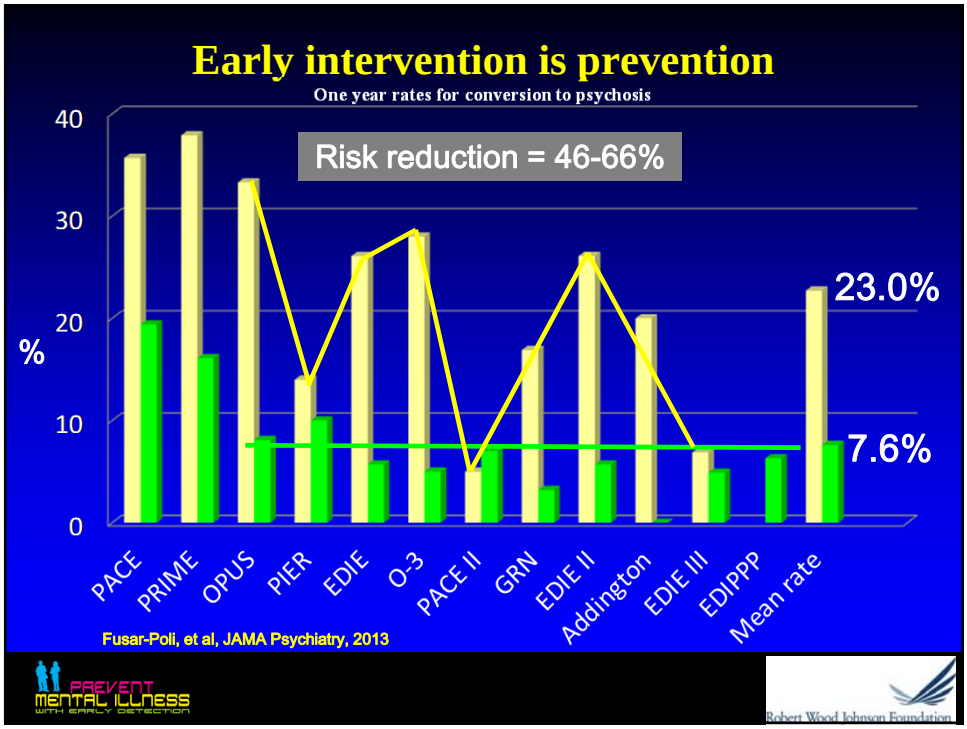
Early intervention is prevention
One year rates for conversion to psychosis
Risk reduction = 46-66%
%
40
30
20
10
0
23.0%
7.6%
PACE
PRIME
OPUS
PIER
EDIE
O-3
PACE II
GRN
EDIE II
Addington
EDIE III
EDIPPP
Mean rate
Fusar-Poli, et al, JAMA Psychiatry, 2013
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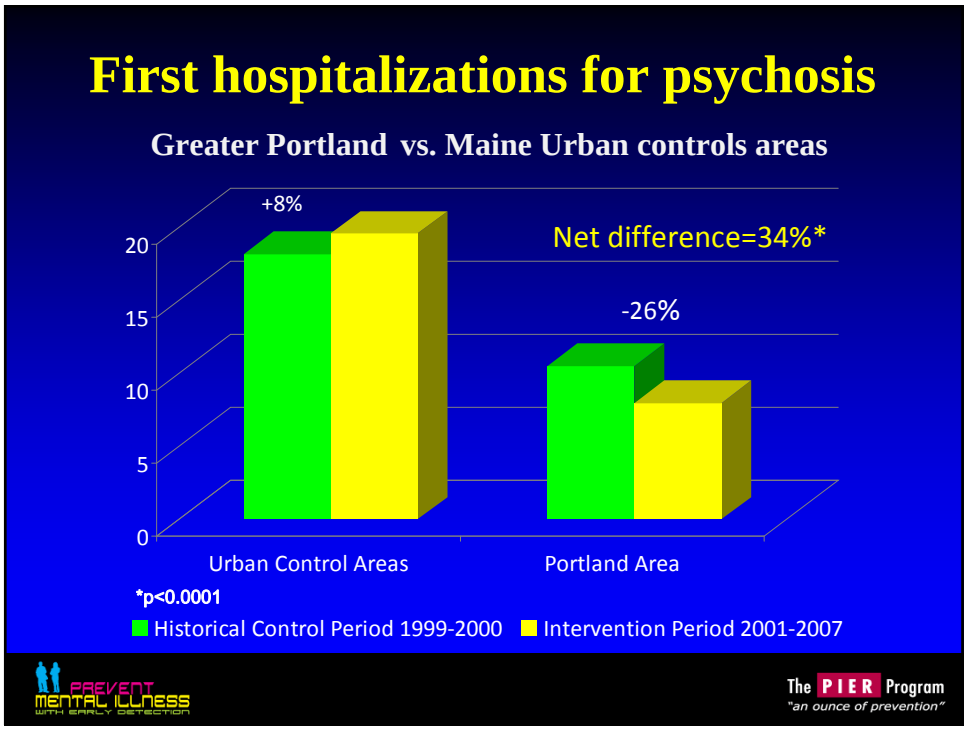
First hospitalizations for psychosis
Greater Portland vs. Maine Urban controls areas
+8%
Net difference=34%*
-26%
20
15
10
5
0
Urban Control Areas
Portland Area
*p<0.0001
Historical Control Period 1999-2000
Intervention Period 2001-2007
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Meta-analyses of RCT of intervention in high-risk samples

For conversion to psychosis

Study	Risk ratio (risk reduction)
• Fusar-poli, et al., 2013	• 0.34 (-66%; n=554)*
• van der Gaag, et al., 2013	• 0.46 (-54%; n=1,112)*
• Stafford, et al., 2013	• 0.54 (-46%; n=1,246)*
• Integrated treatment (Nordentoft, 2006, Bechdolf, 2012)**	• 0.19 (-81%)

*p<0.05

**Integrated treatment includes those studies in which psychoeducational multifamily groups and cognitive therapy or social skills training were provided.

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