Attenuated Psychosis Syndrome
What is it?

David A. Graeber, MD

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Goals & Objectives

1. Proposed Attenuated Psychosis Syndrome
2. Rationale for Proposed Inclusion in DSM-V
3. Research Supporting Inclusion
4. Interventional Studies in Psychosis Risk Syndrome Populations
5. Questions & Comments

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Proposed Attenuated Psychosis Syndrome

All six of the following:

a) Characteristic symptoms: at least one of the following in attenuated form with intact reality testing, but of sufficient severity and/or frequency that it is not discounted or ignored;

   i. Delusions
   ii. Hallucinations
   iii. Disorganized Speech

Proposed Attenuated Psychosis Syndrome

b) Frequency/Currency

symptoms must be present in the past month and occur at an average frequency of at least once per week in past month

c) Progression

symptoms must have begun in or significantly worsened in the past year

d) Distress/Disability/Treatment Seeking

symptoms are sufficiently distressing/disabling to patient/parent/guardian to lead them to seek help

Proposed Attenuated Psychosis Syndrome

e) Symptoms are not better explained by any DSM-V diagnosis, including substance-related disorder

f) Clinical criteria for any DSM-IV psychotic disorder have never been met

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Rationale for APS
Proposed Inclusion in DSM-V

- Outcomes in Schizophrenia and Psychosis
- Duration of Untreated Psychosis (DUP) as a moderator of outcome
- Prodromal phase of schizophrenia
- Psychosis as a continuum

Psychosis – Implications

Psychosis may confer a more severe course of illness

Chicago Follow Up Study (Harrow, Schizophr Bull 2005)

- 15 year prospective study of 274 young (age 23) psychiatric inpatients (Index Admission)
- 64 with Schizophrenia / 12 schizophreniform disorder
- 81 with other psychosis (46% Bipolar Disorder, 35% Unipolar Depressed)
- 117 non-psychotic patients (62% Depressive D/O's)

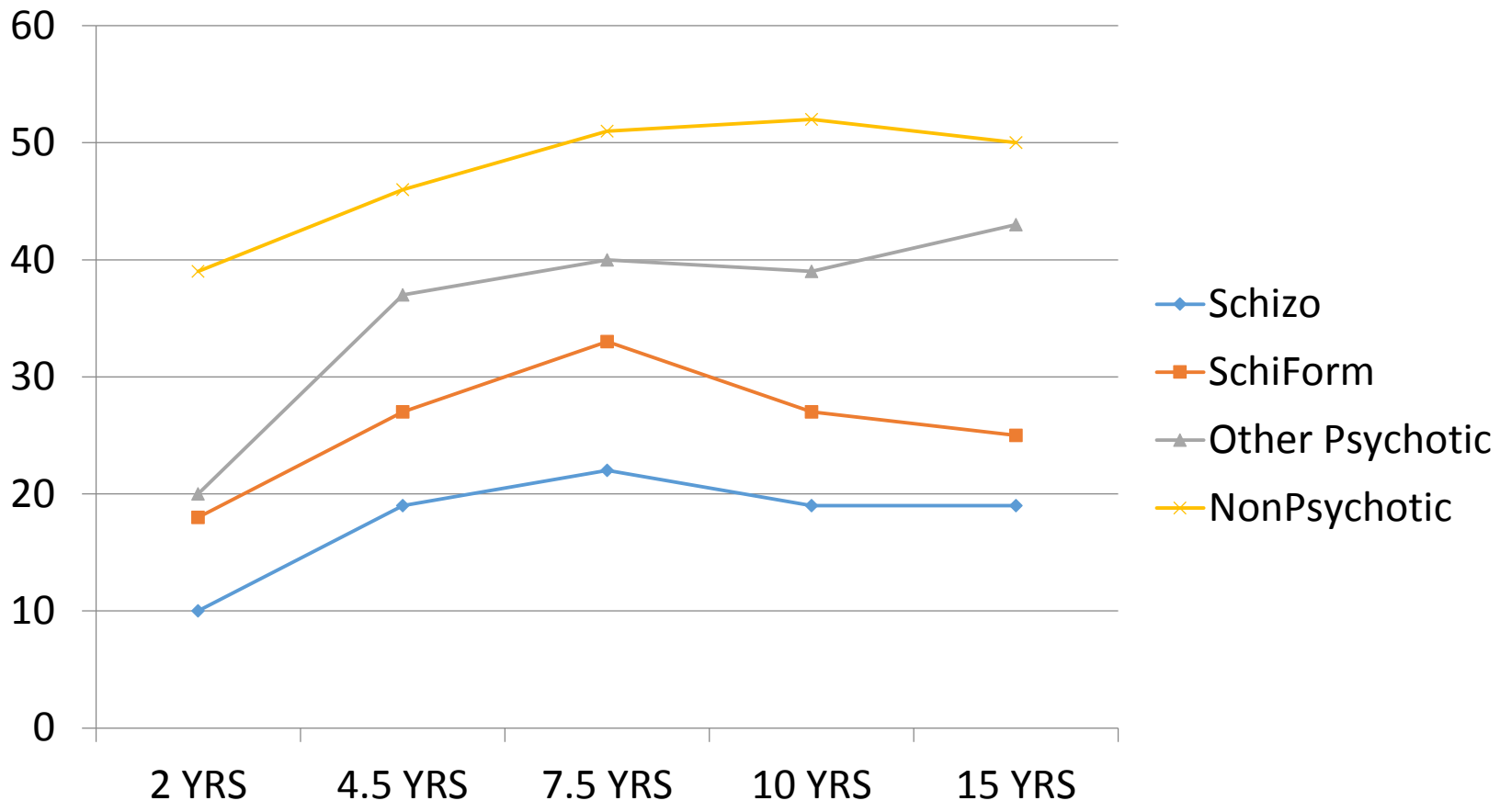
Psychosis – Implications

Chicago Follow Up Study (Harrow, Schizophr Bull 2005)

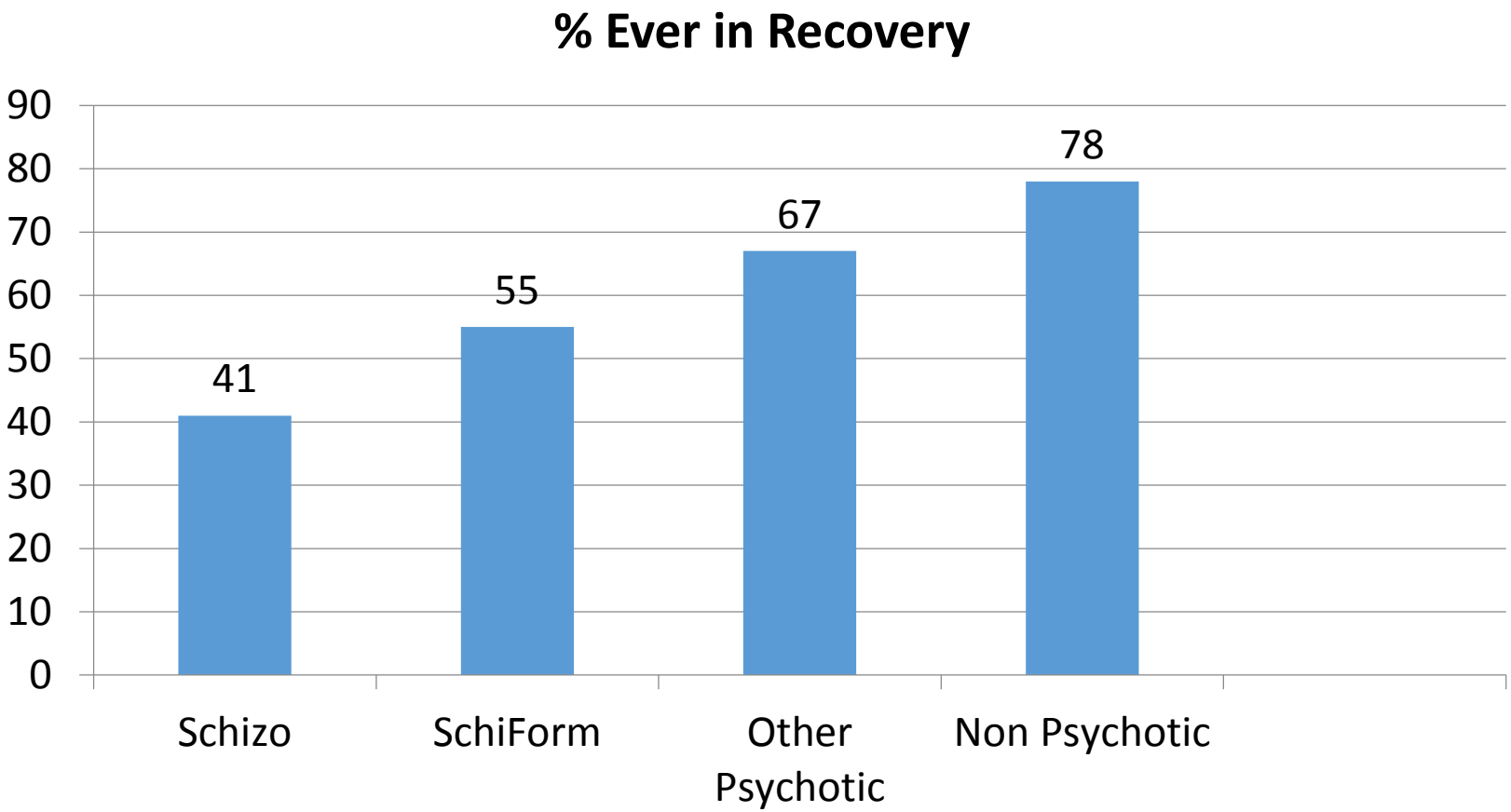
Definition of Recovery for minimum of 1-year in any of 5 follow up periods:

- Absence of psychotic symptoms
- "Adequate" Psychosocial Functioning – instrumental (paid) work at least ½ time
- Absence of very poor social activity level
- No psychiatric admissions

Periods of Recovery
(y-axis % with 1 year recovery in follow up period)



Any 1-Year Period of Recovery in 15 Year Follow Up



DUP as Moderator of Outcome

DUP – time elapsed between onset of frank psychotic symptoms and initiation of treatment

In schizophrenia DUP associated with:

- At time of index treatment – associated with severity of negative symptoms but not general psychopathology, positive symptoms or neurocognitive function

- Response to antipsychotic medication including global psychopathology, positive and negative symptoms and functional outcomes

Perkins D. Am J Psychiatry 2005

DUP as Moderator of Outcome

Outcomes in Schizophrenia

- Shorter DUP predicted Social functioning in 1st first episode patients (FEP) at 1 and 2 year follow up (Addington, Psych Med 2004)
- Shorter DUP in FEP associated with significantly higher levels of functioning at 5, 10, 15 and 20 year follow up with strongest association with DUP < 6 months [Mean DUP 84 weeks] (Kua, Acta Psych Scan 2003)
- Lack of Correlations – No difference in function or symptoms severity at 6 month follow up in neuroleptic naïve FEP; mean DUP 60 weeks (Ho, Am J Psych 2000)

DUP as Moderator of Outcome

Neurocognitive Deficits in Schizophrenia

- Neurocognitive deficits are well established and predicts impairments in functioning even when controlling for positive symptoms
- Deficits include processing speed, verbal & working memory, sustained attention, and executive functions (reasoning, planning, problem solving)
- Study of 102 FEP; DUP (mean 46 weeks) did not predict cognitive deficits at baseline or after 16 weeks of AP treatment (Goldberg, Schizophrenia Res 2009).

Prodromal Phase of Schizophrenia

- Prodromal Phase of Schizophrenia Course has long been recognized

- Significant negative social consequences of schizophrenia emerge in prodromal phase of the illness

Prodromal Phase of Schizophrenia

ABC Study of Schizophrenia

(Hafner, Eur Arch Psych Clin Neuro 1999)

N = 232 FEP – index admission for Schizophrenia

Used IRAOS to assess prodromal phase of illness

- 73% started with non-specific or negative symptoms
- 20% started with positive and negative symptoms
- 7% started with positive symptoms only

Prodromal Phase of Schizophrenia

Most common early signs of illness reported by patient:

Ranking	Sign	Total % N = 232	Men % N = 108	Women % N = 124
1	Restlessness	19	15	22
2	Depression	19	15	22
3	Anxiety	18	17	19
4	Think/Concentration	16	19	14
5	Worrying	15	9	20*
6	Self-Confidence	13	10	15
7	Energy/Slowness	12	8	15
8	Poor Work Performance	11	12	10
9	Social Withdrawal	10	8	12

Psychosis as a Continuum

View that psychosis phenotype is expressed at various levels in a population.

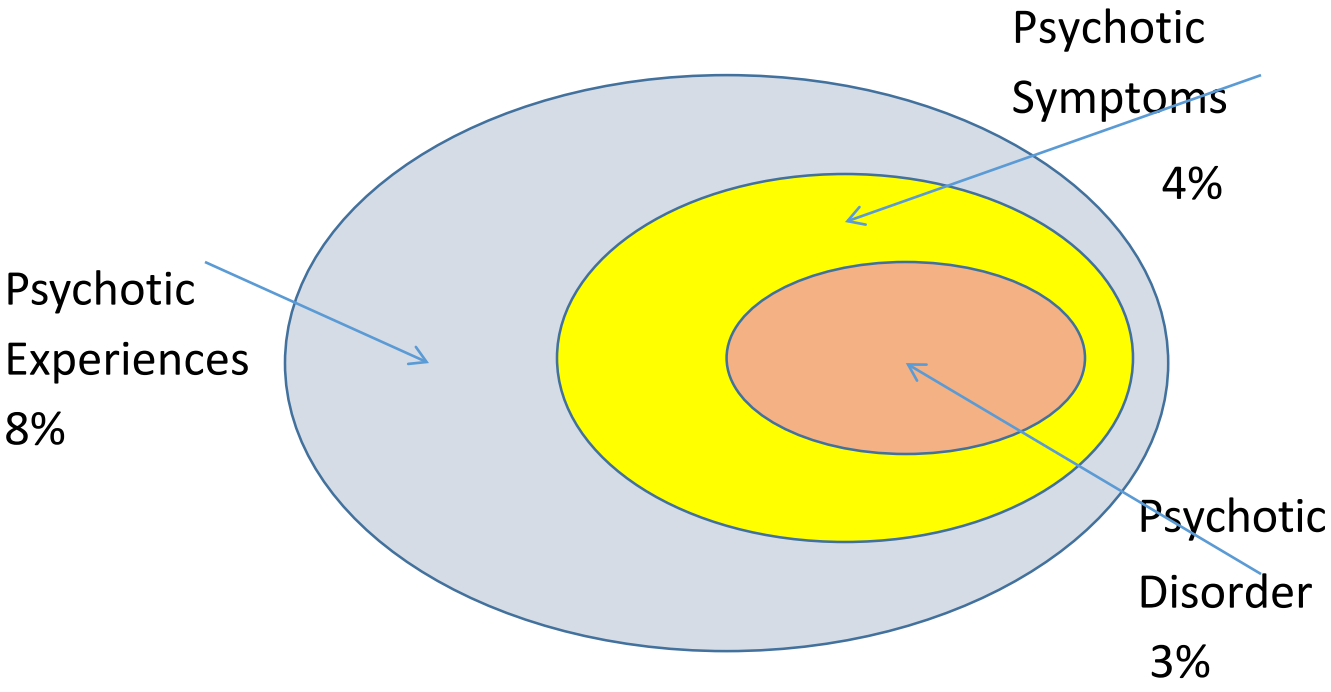
Assumption is that experiencing symptoms of psychosis – such as hallucinations and delusions is not inevitably associated with the presence of a psychotic disorder.

(van Os, Psychological Medicine 2009)

Psychosis as a Continuum

Meta-analysis of 35 cohorts investigating prevalence and incidence of psychotic phenotypes in community samples

(van Os, Psychological Medicine 2009)



Psychosis as a Continuum

Meta-analysis of 35 cohorts investigating prevalence and incidence of psychotic phenotypes in community samples

(van Os, Psychological Medicine 2009)

<u>Summary</u>

Incidence 3%

Prevalence 5%

Majority of psychotic experiences in the population are transitory and disappear in 75% - 90% of individual

Psychosis as a Continuum

Subclinical Psychosis Associations:

Demographic

Males, migrants, ethnic minorities, being unmarried, unemployed and lower levels of education

Non-Genetic Risk

Cannabis, alcohol, traumatic experiences, urbanicity

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Prodromal Risk Assessment

Structured Interview for Prodromal Syndromes (SIPS)

(Miller, McGlashan, Schizophr Bull 2003)

Measures:

- Scale of Prodromal Symptoms (SOPS)
- Schizotypal Personality Disorder Checklist (APA 1994, DSM-IV)
- Family History Questionnaire (Andreasen, Arch Gen Psych 1977)
- Anchored GAF (Hall, Psychsomatics 1995)

Prodromal Risk Assessment

Positive Symptoms

- **Unusual Thought Content/Delusional Ideas**
- **Suspiciousness/Persecutory Ideas**
- **Grandiosity**
- **Perceptual Abnormalities/Hallucinations**
- **Disorganized Communication**

Negative Symptoms

- Social Anhedonia
- Avolition
- Expression of Emotion
- Experience of Emotion & Self
- Ideational Richness
- Occupational Functioning

Disorganization Symptoms

- Odd Behavior & Appearance
- Bizarre Thinking
- Trouble with Focus & Attention
- Personal Hygiene

General Symptoms

- Sleep Disturbances
- Dysphoric Mood
- Motor Disturbances
- Impaired Tolerance to Normal Stress

Prodromal Risk Assessment

Score	Criteria - Suspiciousness/Persecutory Ideas
0 - Absent	
1 – Questionably Present	Wariness
2 - Mild	Doubts about safety. Hypervigilance without clear source of danger.
3 - Moderate	Notions that people are hostile, untrustworthy, and/or harbor ill will easily. Sense that hypervigilance may be necessary. Mistrustful. Recurrent sense that people are thinking or saying negative things about person. May appear mistrustful with interviewer.
4 - Moderately Severe	Clear or compelling thoughts of being watched or singled out. Sense that people intend to harm. Beliefs easily dismissed. Presentation may appear guarded. Reluctant or irritable in response to questioning.
5 – Severe but not Psychotic	Loosely organized beliefs about danger or hostile intention. Skepticism & perspective can be elicited with non-confirming evidence or opinion. Behavior is affected to some degree. Guarded presentation may interfere with ability to gather information in the interview.
6 – Severe & Psychotic	Delusional paranoid conviction (with no doubt) at least intermittently. Likely to affect functioning.

Prodromal Risk Assessment

Attenuated Positive Symptom Syndrome

1. One or more of the 5 SOPS positive items scoring in the prodromal range (3-5)

&

2. Symptoms beginning within the past year or increasing 1 or more points within the past year

&

3. Symptoms occurring at least once/week for past month

Prodromal Risk Assessment

Brief Intermittent Psychotic Symptom Syndrome

1. One or more of the 5 SOPS positive items scoring in the psychotic range (rating of 6)

&

2. Symptoms beginning in the past 3 months

&

3. Symptoms occurring at least several minutes per day at least once/month

Prodromal Risk Assessment

Genetic Risk and Deterioration Syndrome

1. First degree relative with history of any psychotic disorder

or

2. Schizotypal Personality Disorder in patient

&

3. GAF drop of at least 30% over past month vs. prior year

Prodromal Risk Syndrome - NAPLS

North American Prodrome Longitudinal Study

(Woods, Schizophr Bull 2009)

Comparison Groups:

Prodromal Risk	N = 377
Normal Control	N = 196
Help-Seeking Comparison	N = 198
Familial High Risk	N = 40
Schizotypal PDO	N = 49

Prodromal Risk Syndrome - NAPLS

- SIPS administered baseline and every 6 months up to 30 months
- Primary Outcome – time to conversion to psychosis
- Psychosis defined as
  - frank psychotic symptoms with serious disorganization or danger
  - Present for 1 month, at least ½ of days, > 1 hr/day

Prodromal Risk Syndrome - NAPLS

Prodromal Risk Syndrome Cohort:

Classification by SIPS:

- Attenuated Psychosis Syndrome 96%
- Brief Intermittent Psychosis 4%
- Genetic Risk & Functional Decline 0%

Diagnosis at Baseline:

- Mood/Anxiety 69%
- Axis II 44%
- SUD 25%

Prodromal Risk Syndrome - NAPLS

Outcomes – Conversion Rates at 2.5 Years

- Prodromal Risk Syndrome 40% (N = 89)
- Normal Control 0%
- Help-Seeking Comparison 4% (N = 3)
- Familial High Risk 0%
- Schizotypal PDO 36% (N = 8)

Prodromal Risk Syndrome - NAPLS

Diagnosis of Converters:

- Prodromal Risk – Schizophrenia Spectrum (56%), Psychosis NOS (34%), Affective D/O (10%)
- HSC – BPAD (33%), Psychosis NOS (33%), ? (33%)
- SPD – Schizophrenia Spectrum (86%), Affective D/O (7%), Other (7%)

Prodromal Risk Syndrome - NAPLS

Clinical Course of Non-Converters At 2-year follow up:

- 38% had anxiety disorder
- 15% depressive disorders
- Social & role functioning significantly lower than Normal Controls
- 40% still had a least 1attenuated positive symptom

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Intervention Studies - Psychosocial

Cognitive Therapy

Manchester Cognitive Therapy Trial

(Morrison, Schizophr Bull 2007)

N = 56

Cognitive Therapy (CT) vs. Treatment As Usual (TAU)

CT – lower conversion at 6 months; no difference at 3 years

- 20% CT
- 30%TAU

Intervention Studies - Psychosocial

Integrated Treatment

Danish National Schizophrenia Study

(Rosenbaunm, World Psych 2006)

N = 79 Schizotypal PDO

Integrative Treatment vs. TAU

Integrative Therapy included Multifamily Group Therapy, Assertive Community Treatment & Antipsychotic Medication

2 year conversion rates:

- Integrative Treatment 25%
- TAU 48%

Intervention Studies - Pharmacology

Personal Assessment and Crisis Evaluation (PACE)

(McGorry, Arch Gen Psych 2002)

- N = 59 Prodromal Patients ages 14-28
- Compared Needs Based Intervention (NBI) vs. Preventative Intervention (PI - which was NBI + Risperidone + CT)
- Treatment Duration was 6-months
- Mean Risperidone dose was 1.3 mg/day

6 month active treatment conversion rates:

- NBI 10/28 (36%)
- PI 3/31 (10%)

12 month conversion rates (trend but not significant difference):

- NBI 10/28 (36%)
- PI 6/31 (19%)

Intervention Studies - Pharmacology

PRIME Study (McGlashan, Am J Psych 2006)

N = 60 Prodromal Patients (age 12-45)
Olanzapine (N = 31) vs. Placebo (N = 29)
1 year treatment with additional 1 year no treatment follow up

Year 1 Conversion Rates:
- Olanzapine 5/31 (16%) – 17 non-converting patients dropped out
- Placebo 11/29 (38%) – 10 non-converting patients dropped out

Year 2 Additional Conversion Rates:
- Olanzapine 3/9 (33%)
- Placebo 2/8 (25%)

Mean Olanzapine Dose 10.2 mg/day
Weight Gain in Treatment Year = 8.8 Kg

Intervention Studies - Pharmacology

Omega-3 Fatty Acids (PUFA)

(Amminger, Arch Gen Psych 2010)

N = 81 Help Seeking Prodromal Patients (ages 12 to 25)

PUFA vs. Placebo (3 months treatment/9 additional months F/U)

12 month Conversion Rates:

- 2/41 (5%) PUFA
- 11/40 (28%) Placebo

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Comments & Questions

- I would like to see Attenuated Psychosis Syndrome included in DSM-V
- Questions?

DSM-5 Proposed A Criteria for Schizophrenia

Schizophrenia

A. Characteristic symptoms: Two (or more) of the following, each present for a significant portion of time during a 1-month period (or less if successfully treated). At least one of these should include 1-3.

1. Delusions
2. Hallucinations
3. Disorganized speech
4. Grossly abnormal psychomotor behavior, such as catatonia
5. Negative symptoms, i.e., restricted affect or avolition/asociality

Psychotic Disorders Dimensional Scale - DSM-5

	Hallucinations	Delusions	Disorganization	Abnormal Psychomotor Behavior	Restricted Emotional Expression	Avolition
0	Not Present	Not Present	Not Present	Not Present	Not Present	Not Present
1	Equivocal (severity or duration not sufficient to be considered psychosis)	Equivocal (severity or duration not sufficient to be considered psychosis)	Equivocal (severity or duration not sufficient to be considered disorganization)	Equivocal (severity or duration not sufficient to be considered abnormal psychomotor behavior)	Equivocal decrease in facial expressivity, prosody, or gestures	Equivocal decrease in self-initiated behavior
2	Present, but mild (little pressure to act upon voices, not very bothered by voices)	Present, but mild (delusions are not bizarre, or little pressure to act upon delusional beliefs, not very bothered by beliefs)	Present, but mild (some difficulty following speech and/or occasional bizarre behavior)	Present, but mild (occasional abnormal motor behavior)	Present, but mild decrease in facial expressivity, prosody, or gestures	Present, but mild in self-initiated behavior
3	Present and moderate (some pressure to respond to voices, or is somewhat bothered by voices)	Present and moderate (some pressure to act upon beliefs, or is somewhat bothered by beliefs)	Present and moderate (speech often difficult to follow and/or frequent bizarre behavior)	Present and moderate (frequent abnormal motor behavior)	Present and moderate decrease in facial expressivity, prosody, or gestures	Present and moderate in self-initiated behavior
4	Present and severe (severe pressure to respond to voices, or is very bothered by voices)	Present and severe (severe pressure to act upon beliefs, or is very bothered by beliefs)	Present and severe (speech almost impossible to follow and/or behavior almost always bizarre)	Present and severe (abnormal motor behavior almost constant)	Present and severe decrease in facial expressivity, prosody, or gestures	Present and severe in self-initiated behavior