

Management of Recent Onset Psychosis

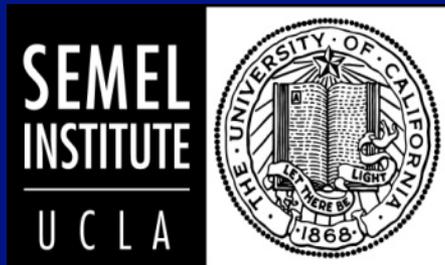
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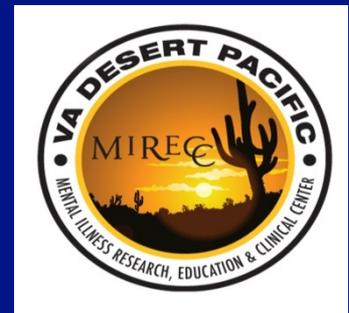
Semel Institute for Neuroscience and Human Behavior at UCLA

**Director, Mental Illness Research, Education, and Clinical Center
(MIRECC)**

Los Angeles, California



**UCDavis/UCLA Behavioral Center of
Excellence Webinar**



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Disclosures:

Consultation for Boeringer-Ingelheim, Lundbeck, Otsuka,
Takeda, Teva, Roche, Genentech, Targacept, Forum,
Allergan

Research Support from Forum, Synchronuron, Neurocrine

Special issues in first-episode patients

- **Diagnostic uncertainty**
- **Concerns about delaying treatment**
- **How long to treat**
- **High rates of suicide**
- **Resistance to settings that serve chronically mentally ill**

Schizophrenia PORT Recommendations

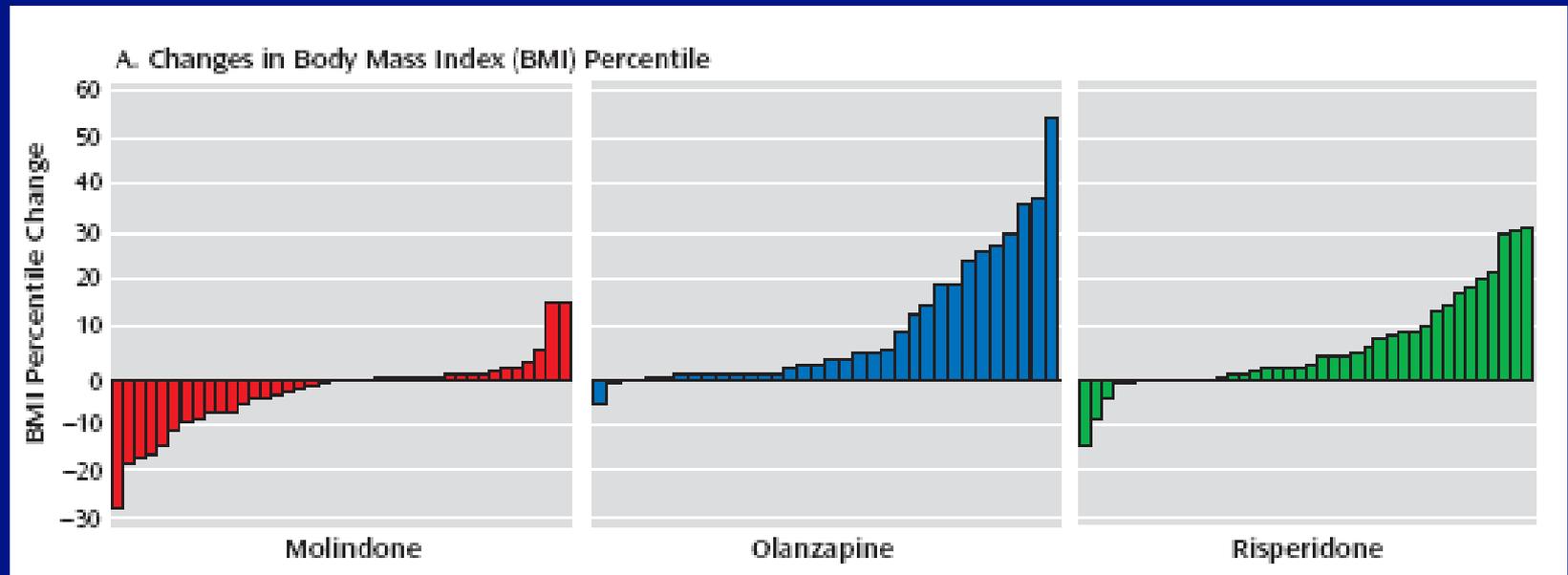
- **People in first-episodes show increased responsiveness and an increased sensitivity to side effects**
- **Doses should be lower than for multi-episode patients**

Treatment of early-onset schizophrenia spectrum disorders (TEOSS)

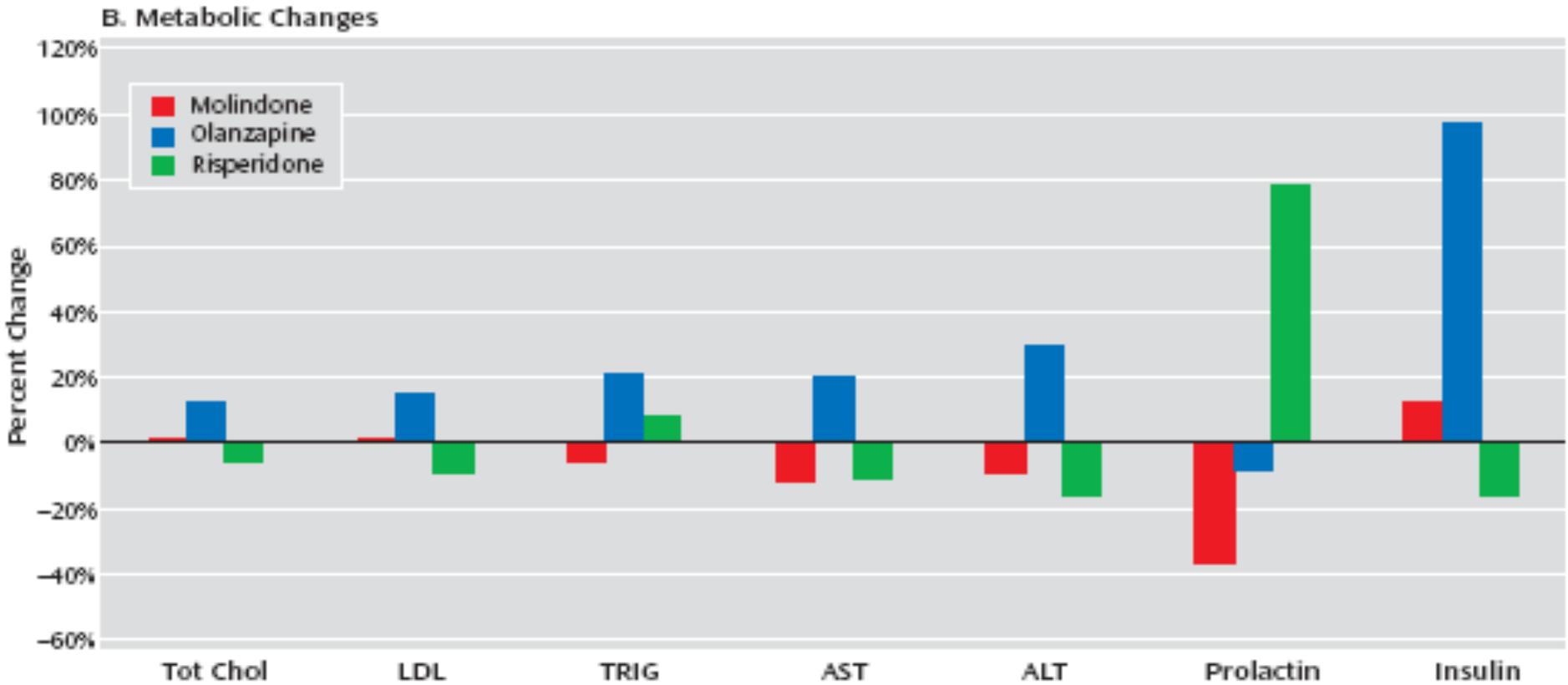
Sikich et al Am J Psychiatry 2008

- **8-19 yo pts w schizophrenia were randomly assigned to double-blind molindone 10-140 mg, olanzapine 2.5-20 mg, or risperidone 0.5-6 mg for 8 weeks**
- **Primary outcome was responder status defined as much or very much improved on CGI; $\geq 20\%$ reduction in total PANSS; and tolerating treatment**

BMI Change in TEOSS



Metabolic Changes in TEOSS



New Recommendations from Schizophrenia PORT (Kreyenbuhl 2010)

*Treatment of Acute Positive Symptoms in People With
First-Episode Schizophrenia: Antipsychotic Medication
Choice*

Recommendation. Antipsychotic medications, other than clozapine and olanzapine, are recommended as first-line treatment for persons with schizophrenia experiencing their first acute positive symptom episode.

Recovery in Remitted First-Episode Psychosis at 7 Years of Follow-up of an Early Dose Reduction/Discontinuation or Maintenance Treatment Strategy

Long-term Follow-up of a 2-Year Randomized Clinical Trial

Lex Wunderink, MD, PhD; Roeline M. Nieboer, MA; Durk Wiersma, PhD; Sjoerd Sytema, PhD;
Fokko J. Nienhuis, MA

- **7 year follow-up of a 2 year randomized trial in first episodes**
- **Those randomized to dose reduction had higher recovery rates and higher functioning.**
- **17 out of 103 patients discontinued antipsychotics. These individuals showed better functioning at 7 years**

Minimizing the burden of antipsychotic medication

- Dose reduction (with supplementation when patients show prodromal or other symptoms)
- Intermittent treatment
- Shared decision-making

Long-Chain ω -3 Fatty Acids for Indicated Prevention of Psychotic Disorders

A Randomized, Placebo-Controlled Trial

G. Paul Amminger, MD; Miriam R. Schäfer, MD; Konstantinos Papageorgiou, MD;
Claudia M. Klier, MD; Sue M. Cotton, PhD; Susan M. Harrigan, MSc; Andrew Mackinnon, PhD;
Patrick D. McGorry, MD, PhD; Gregor E. Berger, MD

**Replication
Attempts:**

**NAPLS
Neuropro**

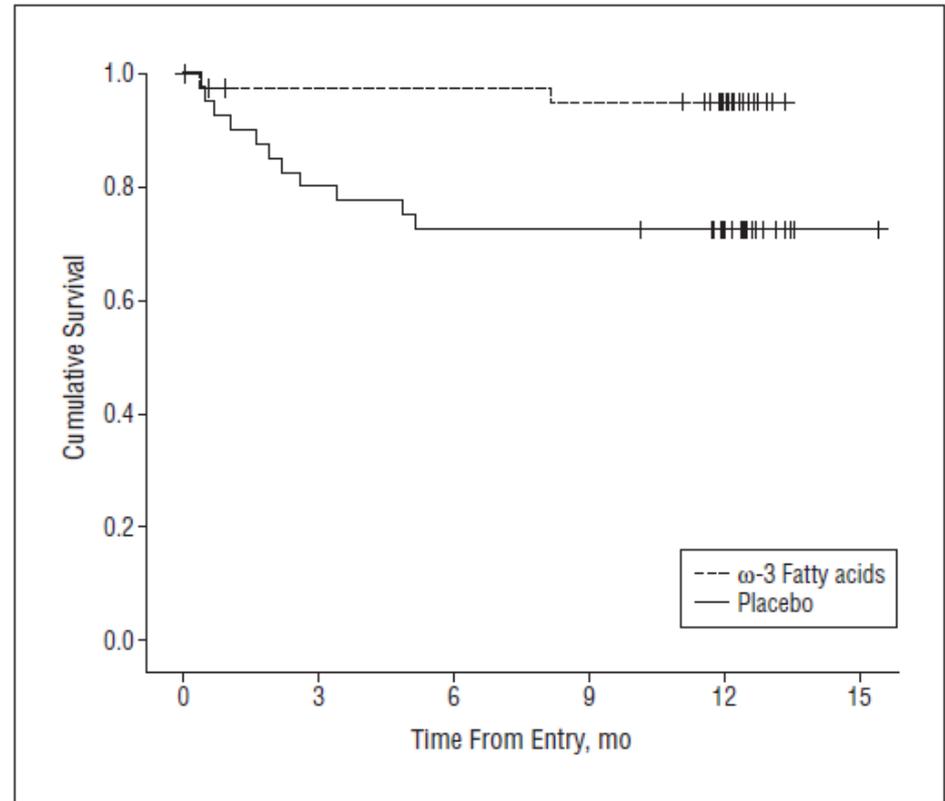


Figure 2. Kaplan-Meier estimates of the risk of transition from the at-risk state to psychotic disorder in patients assigned to ω -3 fatty acids or placebo ($P=.007$ by log-rank test).

Medication Non-Adherence (from Peter Weiden)

- **50% of patients have significant non-adherence within one year of beginning treatment.**
- **75% within two years.**
- **50% of the direct medical costs of psychiatric hospitalization attributed to non-adherence.**

From: Long-Acting Injectable Risperidone for Relapse Prevention and Control of Breakthrough Symptoms After a Recent First Episode of Schizophrenia : A Randomized Clinical Trial

JAMA Psychiatry. Published online June 24, 2015. doi:10.1001/jamapsychiatry.2015.0270

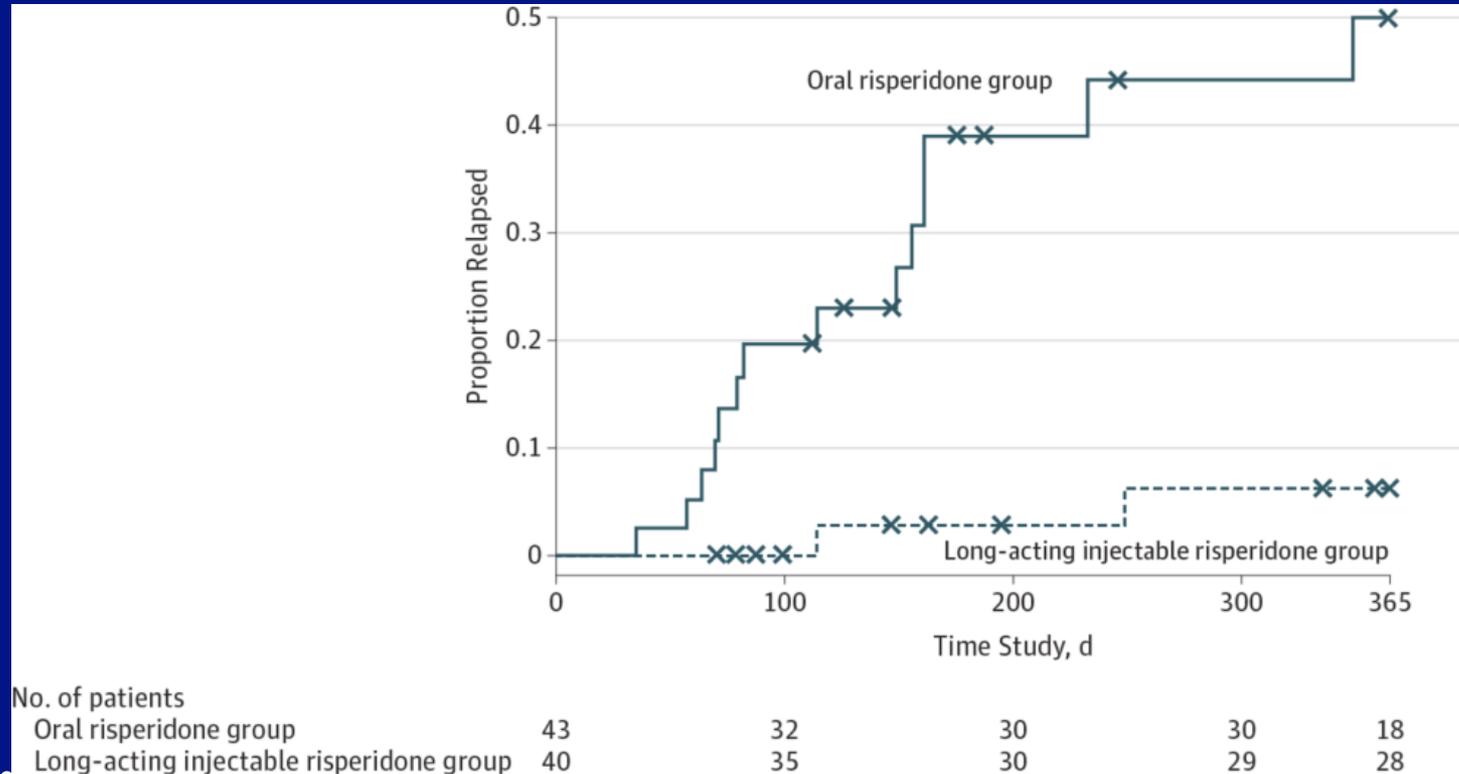


Figure Legend.

Time to First Psychotic Exacerbation and/or Relapse as a Function of Form of Medication Administration in 83 Patients The risk of exacerbation and/or relapse over time was significantly lower for the long-acting injectable risperidone group than for the oral risperidone group. x Indicates censored data.

Early Predictors of Ten-Year Course in First-Episode Psychosis

Svein Friis, M.D., Ph.D., Ingrid Melle, M.D., Ph.D., Jan Olav Johannessen, M.D., Ph.D., Jan Ivar Røssberg, M.D., Ph.D., Helene Eidsmo Barder, Ph.D., Julie Horgen Evensen, M.D., Ph.D., Ulrik Haahr, M.D., Wenche ten Velden Hegelstad, M.Sc., Ph.D., Inge Joa, Ph.D., Johannes Langeveld, Ph.D., Tor Ketil Larsen, M.D., Ph.D., Stein Opjordsmoen, M.D., Ph.D., Bjørn Rishovd Rund, Ph.D., Erik Simonsen, M.D., Ph.D., Per Wiggen Vaglum, M.D., Ph.D., Thomas H. McGlashan, M.D.

TABLE 3. Mixed-model analysis of estimated fixed effects of risk factors for follow-up time in psychosis among 286 patients with *DSM-IV* nonorganic, nonaffective first-episode psychosis^a

Parameter	Estimate	SE	t	df	p	95% CI
Time	.94	.28	3.32	192	.001	.38 to 1.49
Premorbid social deterioration	3.90	1.98	1.97	229	.050	.00 to 7.81
Core schizophrenia spectrum disorder	5.43	2.04	2.67	228	.008	1.42 to 9.45
Duration of untreated psychosis \geq 26 weeks	4.37	2.08	2.10	230	.037	.27 to 8.48
No remission within first 3 months	22.41	2.32	9.65	181	<.001	17.83 to 26.99
No remission within first 3 months \times time	-1.35	.44	-3.08	196	.002	-2.22 to -.49

^a Estimates indicate the reduction of weeks in psychosis per year among those for whom the risk factor was absent compared with those for whom the factor was present.

First-episode psychosis patients should be followed carefully after the start of treatment. Findings indicate that if symptoms do not remit within three months with adequate treatment, there is a considerable risk of a poor long-term outcome, particularly for patients with a deterioration in premorbid social functioning, a DUP of at least half a year, and a diagnosis within the core schizophrenia spectrum.

NICE Guidelines 2013

For children and young people with first episode psychosis offer:

- oral antipsychotic medication in conjunction with**
- psychological interventions (family intervention with individual CBT**

NICE Guidelines 2013

Offer clozapine to children and young people with schizophrenia whose illness has not responded adequately to pharmacological treatment despite the sequential use of adequate doses of at least two different antipsychotic drugs each used for 6–8 weeks.

