

Title: A cluster-randomized large, simple trial to compare long-acting injectable antipsychotic to oral antipsychotics in the early course of schizophrenia

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Methodological Question. Patient-randomized RCTs comparing oral and long-acting injectable (LAI) antipsychotics for schizophrenia have often failed to demonstrate advantages for LAIs. Methodological questions raised by these trials include target population (older and possibly more adherent than usual due to agreeing to treatment randomization) and the effects of the added attention and frequency of visits in an RCT. **Introduction.** The PRELAPSE study addresses these concerns in a cluster-randomized, large simple trial being conducted in the US for patients aged 18 to 35 years with a confirmed SCID-5 diagnosis of schizophrenia and less than five years antipsychotic medication exposure.

Methods. Post randomization, 19 sites offered treatment with the LAI Aripiprazole Once Monthly (AOM) and 20 sites Clinician's Choice (CC) of antipsychotic. Study enrollment was between 12/2014 and 12/2016. Treatment continues for all subjects for up to two years

Results. At CC sites, 344 patients consented, 255 met inclusion criteria and 241 had one or more post-baseline assessments. During screening at AOM sites, only 12.61% of potential subjects refused participation due to the injection requirement. At AOM sites, 328 patients consented, 234 met inclusion criteria, 222 had one or more post-baseline assessments and 212 received at least one AOM injection.

Conclusion. The study addresses the methodological concerns identified above by focusing on patients who are early in the course of illness and patients are aware of their site's treatment allocation at the time of consent. The simple trial design minimizes attention and visit frequency. Results indicate that patients with schizophrenia early in the course of illness can be identified in community clinics, enrolled in an RCT to compare a LAI to oral antipsychotics and that most who consent to LAI treatment will validate that consent by receiving LAI injections.

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