

A RCT of the effects of Medication Adherence Therapy for People with Psychotic Disorders

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(Trial registration: <http://clinicaltrials.gov>, ID: NCT01780116)

Background

- The use of antipsychotic medication in symptom reduction, prevention of relapse and thus improving psychosocial outcomes in schizophrenia and other psychotic disorders is well established [Adams et al., 2005]
- Systematic reviews on clinical trials demonstrate that levels of adherence to oral antipsychotics among these patients is generally poor, ranging from 25-70% [McIntosh et al., 2006]
- While there has been increasing number of patients using *atypical antipsychotics*, little evidence has been found on its increasing psychotic patients' medication adherence [Yamada et al., 2006]

Background

- ‘Adherence’ - the client accepts the advice of healthcare professionals to take medication according to a medical prescription,
 - It reflects the client’s perspective regarding the importance and purpose of taking the prescribed medication
- Various factors affecting antipsychotic medication adherence, e.g., the use of too high dosage and wide variety of medications might result in greater adverse effects and thus reduced adherence or refusals (Medicines Partnership, 2005)

Background

- Appropriate type and dosage of medication should be worked out with individual patients to enhance their adherence
- Recent research also suggested that adherence to medication could be strongly affected by social support, encouragement, and *providing guidance to points of leverage* for improving adherence
 - *Lack of insight into their illness and medication* is the strongest predictor of medication non-adherence (Gray et al., 2002)
 - Better understand and cope with their illness(treatment) may offer potential for improving medication adherence

Background

- Recent literature reviews also indicate that most psycho-education interventions to promote adherence to antipsychotics are *multifaceted and complex*, with limited evidence of their success (McIntosh et al., 2006)
- Motivational interviewing (MI), effectively addressing *attitudinal and behavioural changes*, can increase treatment adherence in schizophrenia



[Ambivalence]:

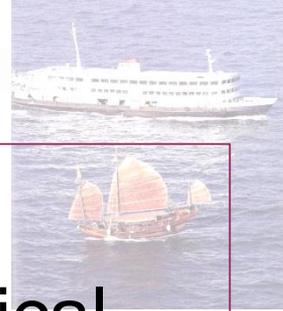
*Unpleasant psychotic sensations moving in and out But **medication** with unwanted side-effects !!*

Aim of The Study

Aim: To test the effectiveness of antipsychotic medication adherence therapy (AT) on clinical outcomes of patients with poor medication adherence in psychosis over 12 months follow-up

Hypotheses:

- Compared with usual outpatient care, at 1 week and 12 months after intervention, the AT would produce significantly greater improvements on patients':
 - Re-hospitalization rate, mental state and adherence rate (**primary outcomes**),
 - Psychosocial functioning and insights into illness/treatment (**secondary outcomes**)



Design

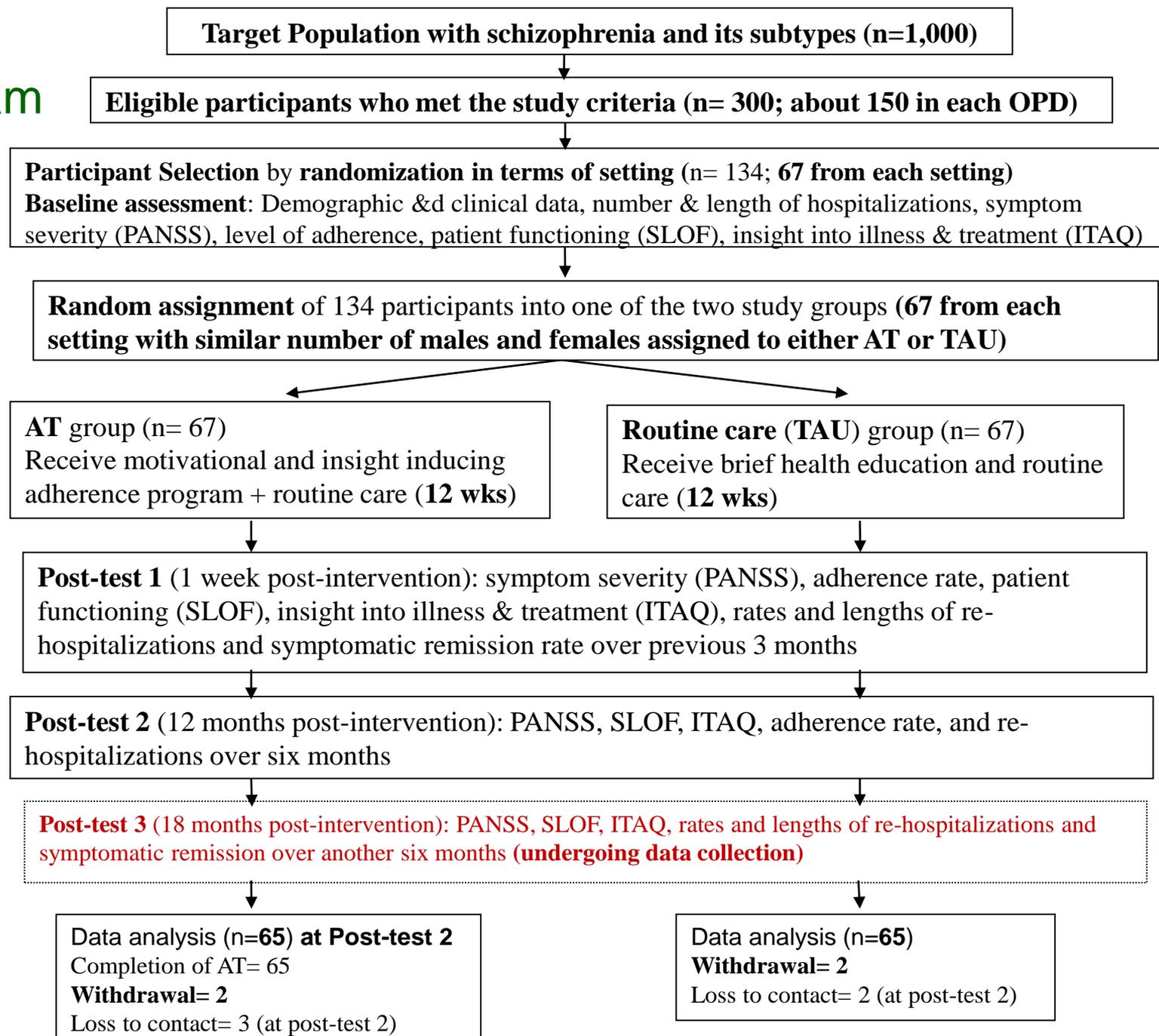


- A randomized controlled trial with single-blind, repeated-measures, control group design
 - Measurements at recruitment and 1 week and 12 months after intervention
- From 2 CPNS, **134** randomly selected patients (aged 18>, primarily schizophrenia):
 - HK Chinese residents, not more than 5 years' illness
 - Global Assessment of Functioning scores of 51>
 - Able to read and understand the questionnaire, training instructions and Cantonese/Mandarin
 - Excluded those receiving other psychotherapies, comorbidity of other severe mental illnesses or medical diseases

Sample size

- 54 patients per intervention to provide 90% power (2-sided $p < 0.05$) to detect a change in symptom severity score of 2.0 points, assuming **one SD=1.5** (Tabachnick & Fidell, 2006); to achieve an average **ES of 0.40** based on 5 RCTs of psycho-education groups in Chinese populations of schizophrenia (Chien et al., 2010, 2012, 2013; Chan et al., 2008; Guo et al., 2010)
- Estimating a 25% attrition rate, **67 patients per arm** will be recruited; after pre-test, randomly assigned into one of two study groups

Flow Diagram of Study Design (I)



Main Content of AT

- Six sessions (biweekly, 2-hour), run by a trained psychiatric nurse, consisting of:
 - 6 principles: expressing empathy, developing discrepancy between client's beliefs and evidence, supporting self-efficacy, avoiding argumentation, and rolling with resistance to behavioral change
 - 3 phases: Engaging participants (1 session; needs assessment & plan for actions); Reviewing strengths and barriers and developing coping strategies (2 sessions); rationalizing beliefs and concerns and preventing relapse (3 sessions)
 - Homework assignment & reviews; risks & coping

Philosophy or Hypotheses of AT

1. Be considered hard to discuss general motivation issues for schizophrenic patients who indicate negative symptoms and pervasive passivity
2. With in-depth behavioral analysis to focus on particular consequences of problem behavior (medication non-adherence), impacting on patients
3. Such consequences serve as opportunities to engage one in discussing ambivalent attitude, which shows promise in improving his/her adherent behavior
4. Self-care and empowerment, partnership in care, and medication experiences, beliefs and attitudes can affect medication adherence

Outcome measures

- Re-hospitalization rate and length of stay over 3-6 months
- Mental state – Positive and Negative Syndrome Scale (**PANSS**) (Kay, Fiszbein & Opler, 2007)
- Level of Adherence - Adherence Rating Scale (**ARS**) (Hayward et al., 1995)
- Insights into illness - Insights and Treatment Attitude Questionnaire (**ITAQ**) (McEvoy et al., 1989)
- Patient functioning – Specific Level of Functioning Scale (**SLOF**) (Schneider & Struening, 1983)

Data Analysis - Outcomes

- Attendance and drop-outs of patients in the AT were recorded.
- *Homogeneity* of the 2 groups examined by comparing the socio-demographic data and baseline outcome scores between groups, using Chi-square or T test
- *Repeated-measures ANOVA* followed by *Helmert's contrasts test* to assess any differences on all outcome variables within & between groups across 2 post-tests (1 week and 12 months follow-up)
- Data analyzed on an *intention-to-treat* basis

Results - Demographics

	AT group (n=65)	Usual care Group (n=65)	Chi-square or t-test (p value)
Gender			1.21 (0.25)
Male	36 (55.4%)	34 (52.3%)	
Female	29 (44.6%)	31 (47.7%)	
Age	30.31 (SD=10.09)	31.92 (SD=11.12)	
Employment			1.12 (0.30)
Employed	35 (53.8%)	31 (47.7%)	
Unemployed	30 (46.2%)	34 (52.3%)	
Education			1.38 (0.18)
Primary	3 (4.6%)	5 (7.7%)	
Secondary	37 (56.9%)	40 (61.5%)	
Tertiary or above	25 (38.5%)	20 (30.8%)	
Living Condition			1.01 (0.35)
Alone	7 (10.8%)	9 (13.8%)	
With family	52 (80.0%)	51 (78.5%)	
Supervised hostel	6 (9.2%)	5 (7.7%)	

Demographics (cont'd)

	AT group (n=65)	Usual care Group (n=65)	Chi-square or t-test (p value)
Clinical diagnosis			1.30 (0.28)
Schizophrenia	33 (50.8%)	35 (53.8%)	
Schizotypal and delusional disorders	27 (41.5%)	22 (33.9%)	
Mood disorders with psychosis	5 (7.7%)	8 (12.3%)	
Duration of illness (years)	2.83 (SD=3.20)	3.05 (SD=4.01)	t= 2.01 (0.11)
Duration of antipsychotics used (years)	1.89 (SD=1.64)	2.06 (SD=1.98)	t= 1.45 (0.18)
No. of psychiatric admissions before intervention			1.02 (0.39)
0	17 (26.2%)	16 (24.6%)	
1	40 (61.5%)	39 (60.0%)	
>=2	8 (12.3%)	10 (15.4%)	
Average number of admissions	1.14 (SD=0.92)	1.38 (SD=1.60)	t= 2.56 (0.09)

Main outcomes

Study Outcome	<u>AT Group (n=65)</u>		<u>Usual Care Group (n=65)</u>		(F[2,121])	P	Effect size (Partial η^2)
	Mean	s.d.	Mean	s.d.			
ITAQ (0 – 33)							
Time 1	14.3	3.0	14.7	2.9	6.52	0.001	0.25
Time 2	16.5	2.9	13.8	3.9			
Time 3	17.8	3.8	13.2	4.0			
SLOF (43 – 215)							
Time 1	138.1	13.8	133.8	16.1	4.98	0.004	0.23
Time 2	147.0	20.1	130.8	21.1			
Time 3	153.3	20.0	128.1	24.9			
PANSS (30 – 210)							
Time 1	80.6	10.9	82.6	12.0	4.36	0.01	
Time 2	64.8	9.2	84.9	13.0			0.18
Time 3	60.2	10.2	84.0	16.4			
Re-hospitalisation							
<i>Frequency</i>							
Time 1	2.8	1.6	2.7	1.0	2.78	0.096	0.05
Time 2	2.4	1.3	2.6	1.2			
Time 3	2.1	1.4	2.7	2.0			
<i>Duration (days/mth)</i>							
Time 1	19.0	6.3	19.2	5.1	4.80	0.004	0.23
Time 2	15.7	5.9	19.8	5.8			
Time 3	13.1	4.6	18.8	5.9			

Level of Adherence

	<u>AT Group (n=65)</u>			<u>Usual Care Group (n=65)</u>		
	Baseline	Post-test 1	Post-test 2 (n=63)	Baseline	Post-test 1	Post-test 2 (n=62)
Adherence Rating						
1. Non-adherent	8 (12.3%)	2 (3.1%)	2 (3.2%)	9 (13.9%)	9 (13.9%)	8 (12.7%)
2. Poor	18 (27.7%)	11 (16.9%)	6 (9.5%)	19 (29.2%)	20 (30.8%)	19 (30.2%)
3. Inadequate	20 (30.8%)	15 (23.1%)	13 (20.6%)	19 (29.2%)	20 (30.8%)	20 (31.8%)
4. Fair	18 (27.7%)	27 (41.6%)	28 (44.4%)	18 (27.7%)	15 (23.1%)	13 (20.6%)
5. Good	0 (0 %)	7 (10.7%)	14 (22.2%)	0 (0 %)	1 (1.5%)	2 (3.2%)

(General Estimating Equation test, Wald's Chi-square= 4.84, p=0.001)

Mean Adherence Rating	2.80 (SD=1.27)	3.58 (SD=1.22)	3.96 (SD=1.01)	2.70 (SD=1.38)	2.91 (SD=1.29)	2.62 (SD=1.40)

(F[2,121]= 4.01, p=0.001) Effect size= 0.27

Discussion

- The AT participants reported significantly greater improvements in: **psychiatric symptoms, psychosocial functioning, insight into illness/treatment, and rehospitalisation duration** over 12 months, compared to usual care. *This model appears to be a promising approach to treatment for Chinese patients with psychotic disorders, similar to that tested by Gray et al. (2006, 2014) in Europe.*
- This motivational therapy group can enhance **patients' insight into illness/ treatments** and reduce lengths of hospitalisation and similar to other psycho-education groups, improve **patients' symptoms and functioning.**

Discussion

- Motivational and insight training can yield improvements **without any increased demand for community mental health services (*cost-saving!*?)**.
- The group program can address not only insight into medication but also **specific cultural needs (e.g., self-blame on having mental illness [*positive thoughts and guilty feeling*] & attitudes and beliefs towards mental illness)** (Ma & Teasdale, 2004)
- In addition to the large effect sizes (partial $\eta^2 = 0.18 - 0.27$) in most outcomes, high attendance (average 5 sessions) **and completion** (2 in-completed) and **low drop-out** (2%) rates reflected its *usefulness and acceptability*

Limitations

- Only Chinese patients were recruited from two psychiatric outpatient clinics in one geographical region in Hong Kong.
- This sample may not be representative of those with *chronic schizophrenia* and *other severe mental illness*, or those with a *co-morbidity* of other mental health problems.
- The motivational and insight-inducing group was time-limited to 3 months and used a less structured and comprehensive format than psycho-education programs; and no booster session was offered.

Potential implications

- Add evidence on the effectiveness of approaches to psychosocial intervention for schizophrenia in adjunct to routine outpatient care, compared to usual psychiatric care
- Address the significance of *insight*, perception, knowledge, and management of medication/illness in early-stage schizophrenia (< 3 yrs of illness)
- Comprehensive assessment of patient outcomes, over a *longer-term follow-up* (>12 months)

Conclusion

The findings of this RCT provide evidence of the effectiveness of a community based AT for psychotic disorders in improving medication adherence, mental state and insight into treatments receiving, hence reducing risk of relapse.

Further RCT in multiple centers and diverse patient groups, as well as over a longer-term follow-up, is recommended.



Thank you!



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