Continuità della cura e innovazione nell'integrazione farmacoterapia-riabilitazione

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Schizophrenia—Time to Commit to Policy Change

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Care and outcomes for people with schizophrenia have improved in recent years, but further progress is needed to help more individuals achieve an independent and fulfilled life. This report sets out the current need, informs policy makers and all relevant stakeholders who influence care quality, and supports their commitment to creating a better future. The authors recommend the following policy actions, based on research evidence, stakeholder consultation, and examples of best practice worldwide. (1) Provide an evidence-based, integrated care package for people with schizophrenia that addresses their mental and physical health needs. (2) Provide support for people with schizophrenia to enter and to remain in their community, and develop mechanisms to help guide them through the complex benefit and employment systems. (3) Provide concrete support, information, and educational programs to families and carers on how to enhance care for an individual living with schizophrenia in a manner that entails minimal disruption to their lives. (4) All stakeholders, including organizations that support people living with schizophrenia, should be consulted to regularly revise, update, and improve policy on the management of schizophrenia. (5) Provide support, which is proportionate to the impact of the disease, for research and development of new treatments. (6) Establish adequately funded, ongoing, and regular awareness-raising campaigns that form an integral part of routine plans of action. Implementation of the above recommendations will require engagement by every stakeholder, but with commitment from all, change can be achieved.

Schizophrenia Bulletin vol. 40 suppl. no. 3 pp. S165–S194, 2014

Schizophrenia—Time to Commit to Policy Change

Table 1. Potential Benefits and Limitations of Current Antipsychotic Medication

Benefits	Limitations
• Reduction of positive symptoms • Treatment of acute episodes • Reduced risk of relapse • Provision of stability and a platform for other treatments • Reduction of aggression and hostility • Reduced suicidal behavior	• Limited efficacy against negative symptoms • Inadequate treatment of cognitive impairment • Troubling side effects or tolerability issues • Low acceptability to some patients – Poor adherence – Negative perceptions

Schizophrenia Bulletin vol. 40 suppl. no. 3 pp. S165–S194, 2014

Comparative efficacy and tolerability of 15 antipsychotic drugs in schizophrenia: a multiple-treatments meta-analysis

Stefan Leucht, Andrea Cipriani, Loukia Spineli, Dimitris Mavridis, Deniz Örey, Franziska Richter, Myrto Samara, Corrado Barbui, Rolf R Engel, John R Geddes, Werner Kissling, Marko Paul Stapf, Bettina Lässig, Georgia Salanti, John M Davis

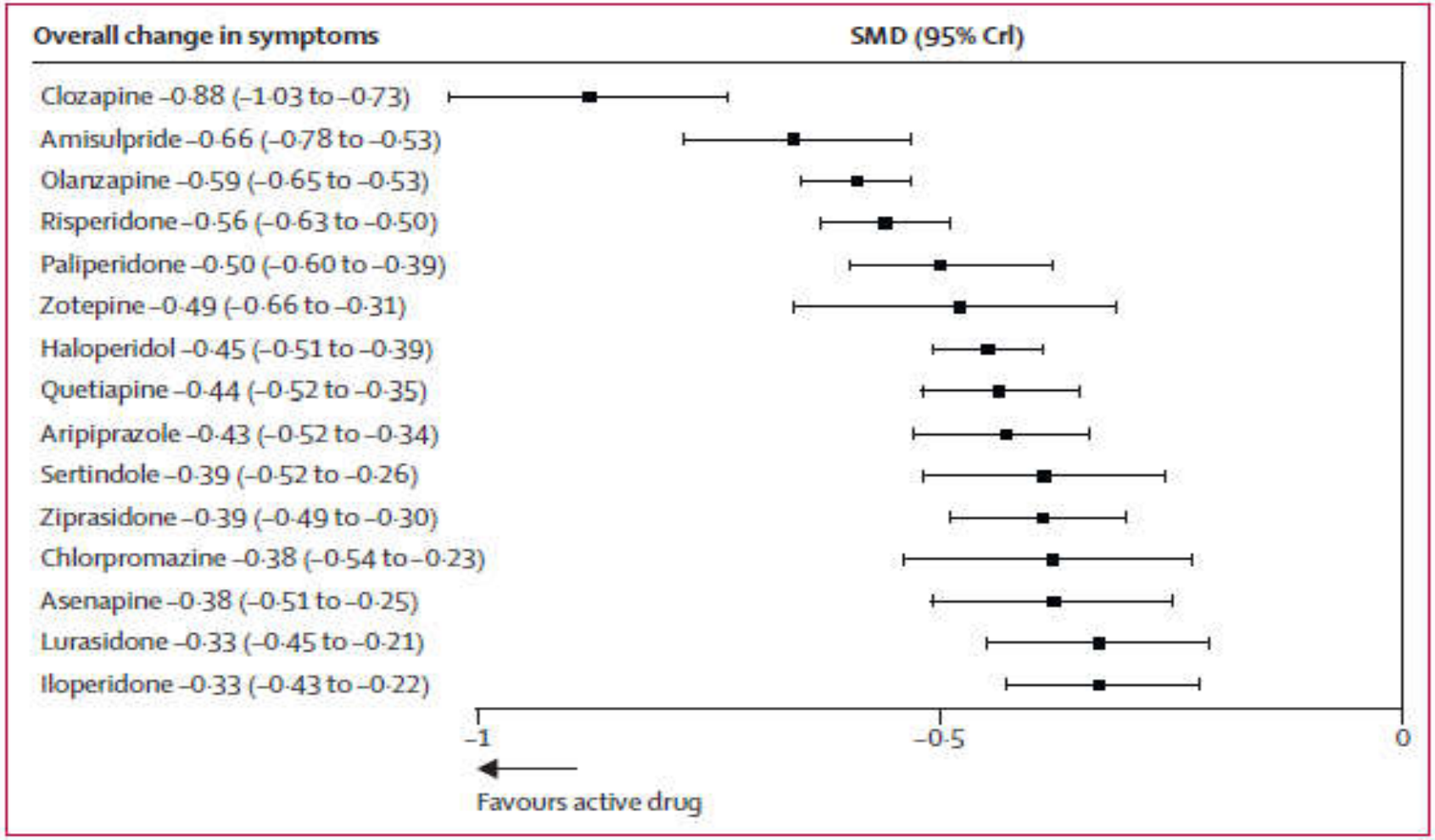
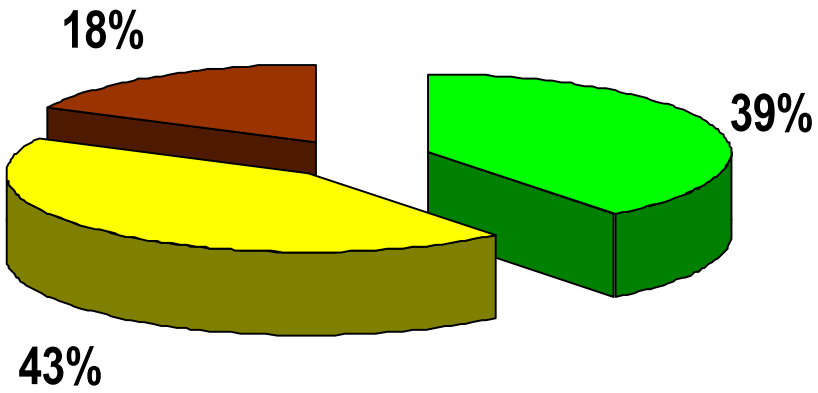


***Figure 3*: Forest plot for efficacy of antipsychotics drugs compared with placebo**
Treatments are ranked according to their surface under the cumulative ranking (SUCRA) values (appendix p 98). SMD=standardised mean difference. CrI=credible interval.

Lancet 2013; 382: 951–62

What proportion of Schizophrenic patients are adherent?



N=34,128, VA sample
Mean age 51 years, predominantly male.
Adherence measured from mean possession ratio

Valenstein, et al. (2006) J Clin Psychiat, 67: 1542-50.

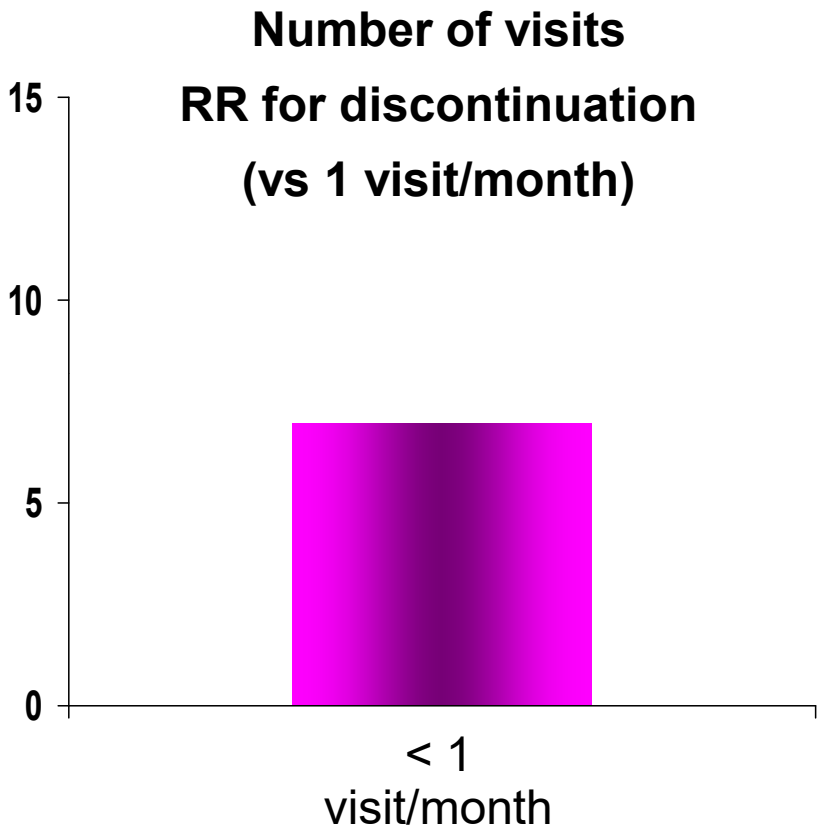
Medication Adherence and Long-Term Functional Outcomes in the Treatment of Schizophrenia

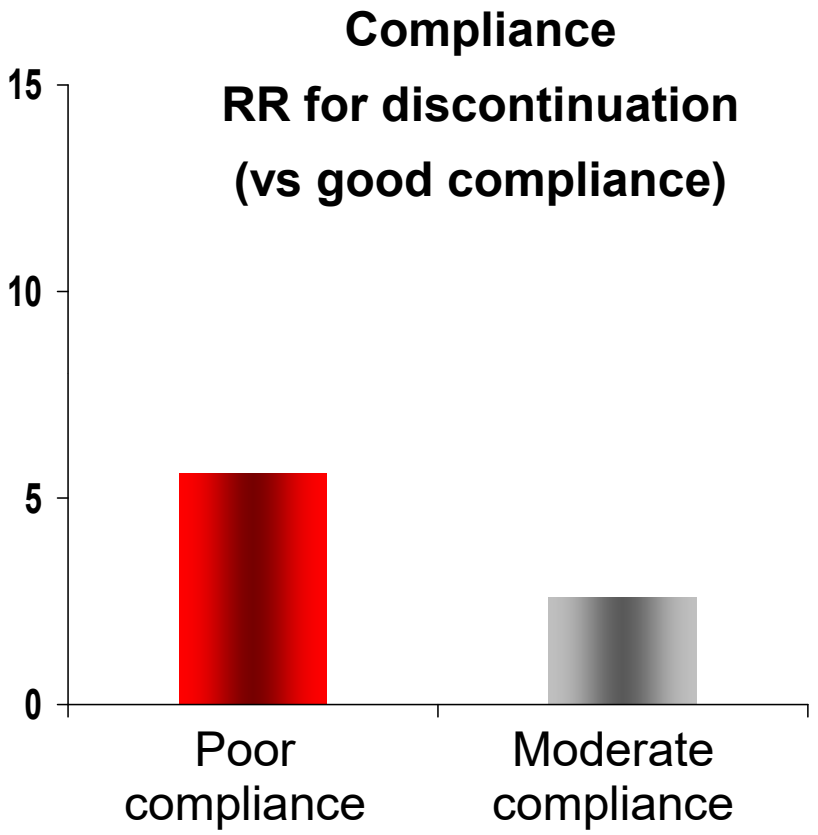
Nonadherence was associated with poorer functional outcomes, including greater risk of hospitalizations, use of emergency psychiatric services, arrest, violence, poorer life satisfaction, greater substance abuse and more alcohol-related problems (all $p<.001$).

Nonadherence in the first year predicted significantly poorer outcomes in the following two years.

Ascher-Svanum H et al, J Clin Psychiatry 2006; 67: 453-60

Factors affecting discontinuation of antipsychotics in patients with schizophrenia: a 18-month, retrospective, real-world study





Vita A et al., (2008) Schizophrenia Res, 104:302-4.

Strategies to improve adherence

- More frequent and longer visits
- Patient and family psychoeducation
- CB interventions and motivational interview
- Social interventions

- Pharmacological interventions
  - Increase or decrease the dose of current antipsychotic
  - Add medications for side effects
  - Monitor plasma levels of medication (especially if oral)
  - Simplify medication regimen
  - Switch to a long-acting antipsychotic

Oral versus depot antipsychotic drugs for schizophrenia. A critical systematic review and meta-analysis of randomised long-term trials.

Leucht C, Heres S, Kane JM, Kissling W, Davis JM, Leucht S.

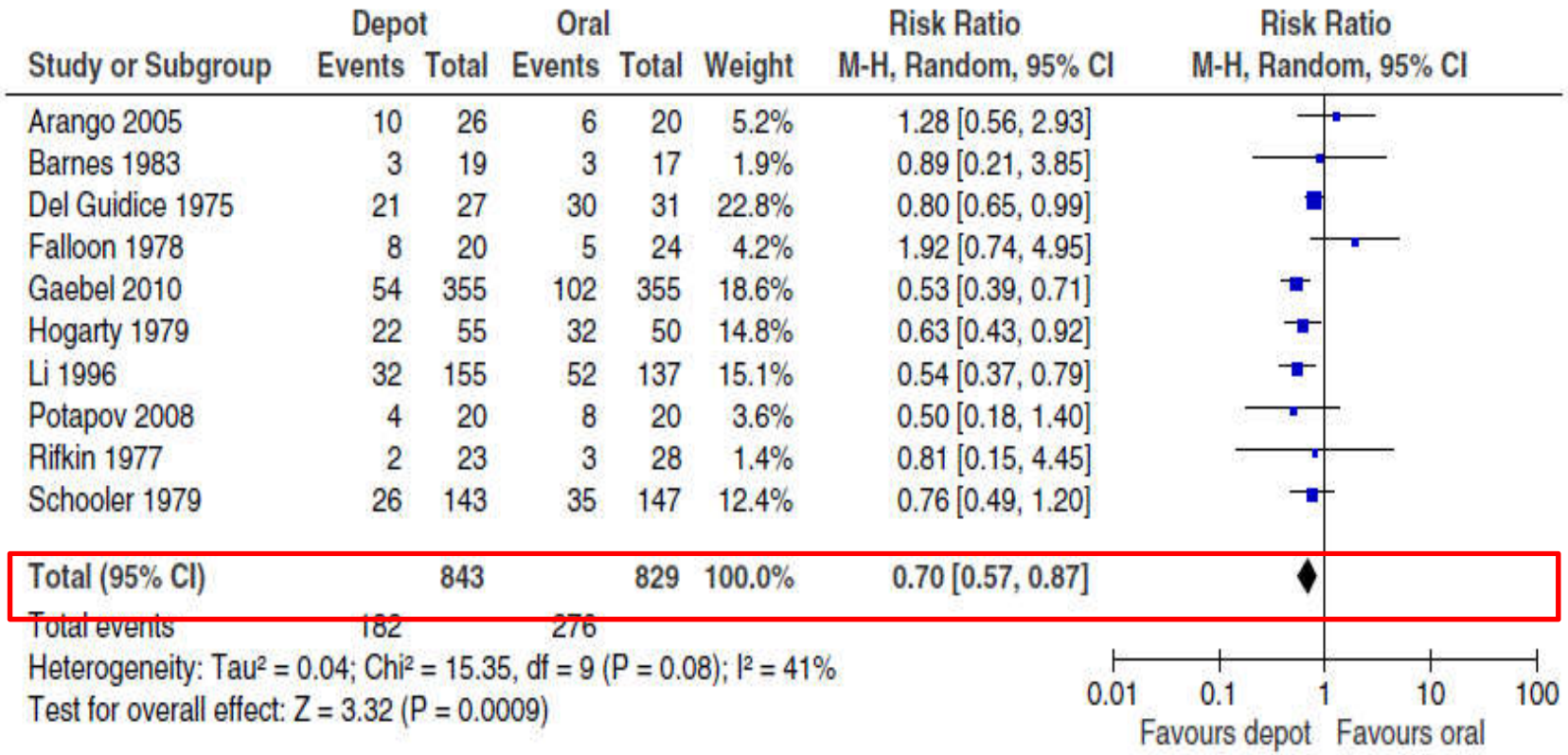


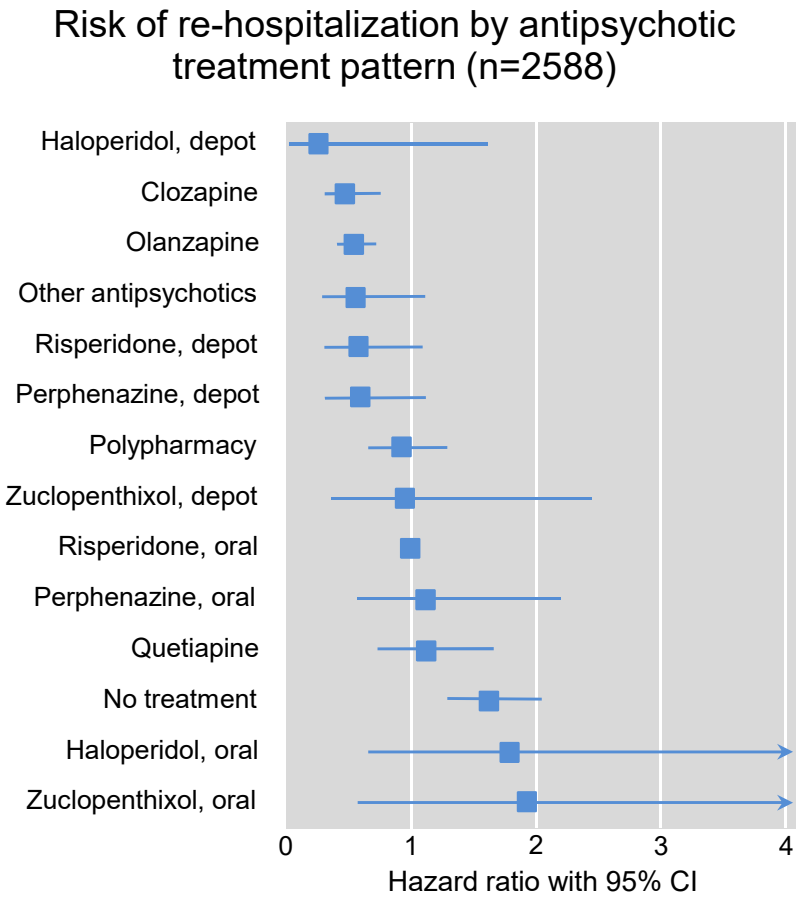
Fig. 1. Relapse footnote: in Li et al. the allocation of 28 out of 320 participants was unclear, reducing the total number of participants from 1700 to 1672. Events = the number of participants with a relapse, Total = the total number of participants in this group.

Schizophr Res. 2011 Apr;127(1-3):83-92. Epub 2011 Jan 22.

Impact of LAI in the early phases of schizophrenia: evidence from pharmacoepidemiological study

- Risk of re-hospitalization in nationwide cohort of 2,588 consecutive patients hospitalized for the first time with a diagnosis of schizophrenia (2000 to 2007) in Finland
- Data obtained from national databases of hospitalization, mortality and AP prescriptions[a]

Risk of re-hospitalization for patients receiving LAI medications was about one-third of that for patients receiving oral medications[b]



[a]Calculated hazard ratios were adjusted for effects of sociodemographic and clinical variables, temporal sequence of APs used, and the choice of the initial AP for each patient; [b]Pairwise comparison [adjusted hazard ratio=0.36, 95% CI=0.17–0.75)]

Tiihonen et al. Am J Psychiatry 2011;168:603–609

Characteristics of Second Generation LAI antipsychotics

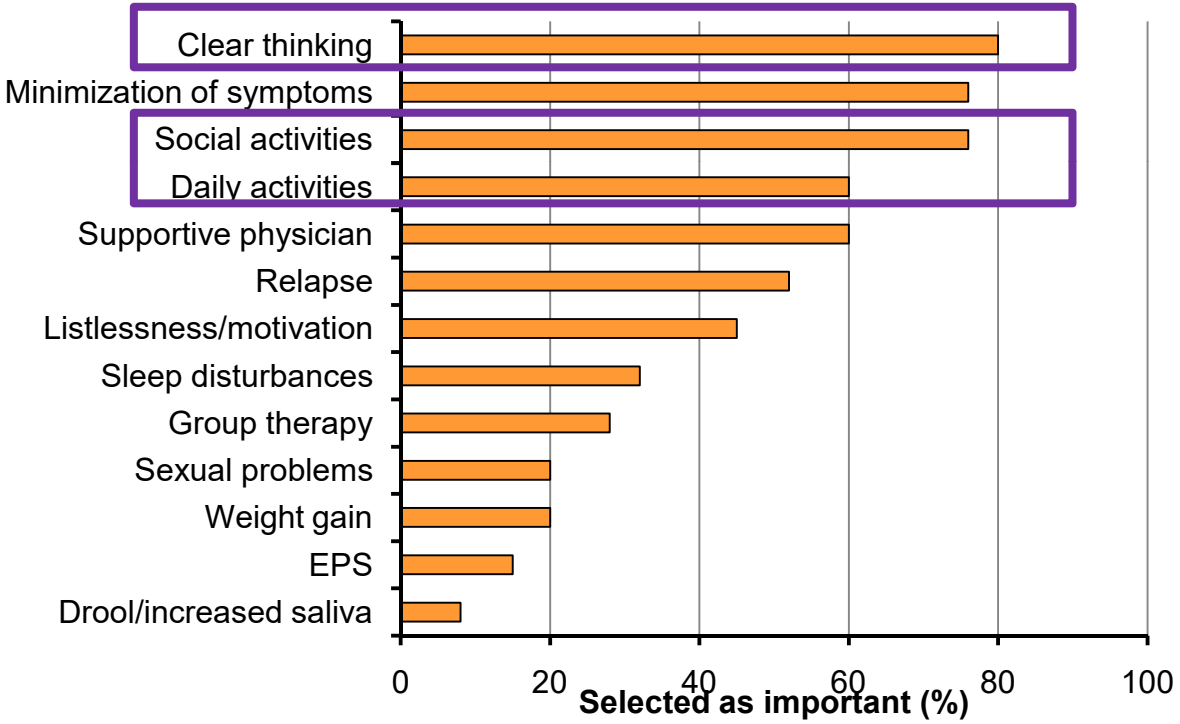
Agent	Formulation	Release mechanism	Available doses	Injection site (IM) according to SPC	Starting modalities	Injection interval	Dose range	T max	T ½ (multiple dosing)	Supply	Needle supplied or recommended	Storage	Monitoring post injection
Risperidone LAI	Aqueous suspension; risperidone encapsulated into biodegradable microspheres	Microspheres: diffusion and erosion	12.5, 25,37.5 or 50 mg	Deltoid or gluteal	It is required a period of 3 weeks of overlap with oral risperidone	2 weeks	12.5-50 mg	21 days	3-6 days	Must be reconstituted: vial with microspheres and syringe with 2 ml of diluent	Deltoid: 21 G 1-inch (25 mm) UTW; Gluteal: 20 G 2-inch (50 mm) TW	Refrigeration is required; (2-8° C)	No
Olanzapine pamoate	Micro-crystalline salt of olanzapine and pamoic acid suspended in aqueous solution	Dissociation into olanzapine and pamoic acid	210, 300 or 405 mg	Gluteal	Several strategies for the LD	2-4 weeks	150-405 mg	7 days	30 days	Must be reconstituted	19 G (38 or 50 mm)	Refrigeration is not required; room temperature (15- 30° C)	Yes (3 hours)
Paliperidone Palmitate	Nanocrystal molecules in aqueous suspension	Poorly soluble in water: hydrolysis by esterases, dissociation into paliperidone and palmitic acid	39, 78, 117, 156, or 234 mg	Deltoid or gluteal	Initial injection on day 1 and day 8. OS not necessary	4 weeks	39-234 mg	13 days	25-49 days	Pre-filled syringes	Deltoid: 23 G 1-inch (25 mm) or 22 G 2 ½-inch (according to patient weight) Gluteal: 22 G 1 ½-inch (38 mm)	Refrigeration is not required; room temperature (15- 30° C)	No
Aripiprazole monohydrate	Aqueous suspension; lyophilized powder of aripiprazole monohydrate crystals	Poorly soluble in water: crystals particles dissociate, with slow and prolonged dissolution and absorption.	300 or 400 mg	Gluteal	OS is necessary for 2 weeks	4 weeks	300 or 400 mg	6.5-7.1 days	29.9-46.5 days	Must be reconstituted	21 G 1 ½-inch (38 mm) in non-obese patients; 21 G 2-inch (50 mm) in obese patients.	Refrigeration is not required; room temperature (15- 30° C)	No

G= gauge; IM= intramuscular; LD= loading dose; OS= oral supplementation; TW= thin wall; UTW= ultra-thin wall

Sacchetti E, Grunze H, Leucht S, Vita A: EBPC 1(1), 24-33

Patient priorities for treatment endpoints

- Individual interviews with patients, discussing endpoints identified in focus groups
- Patients were asked to explain the meaning of each endpoint with respect to their own experience
  - Identified irrelevant and relevant endpoints
  - Selected and ranked five most important endpoints from those identified as relevant

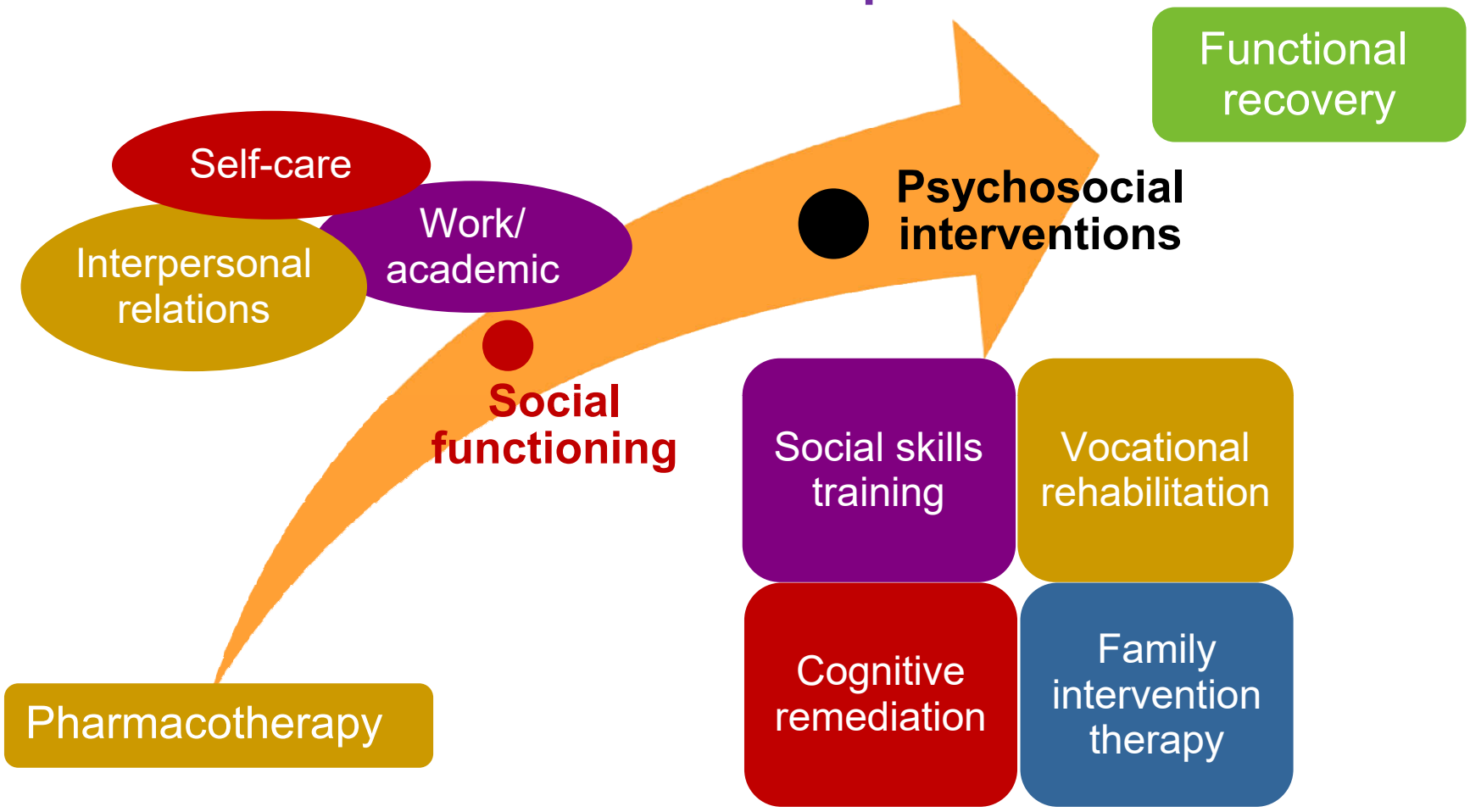


Social activities and daily activities are important to patients with schizophrenia

Selected as important: respondents (%) who selected an endpoint as relevant and also ranked it within their top five of these endpoints Daily activities were defined as maintaining a household, employment and attending and finishing university

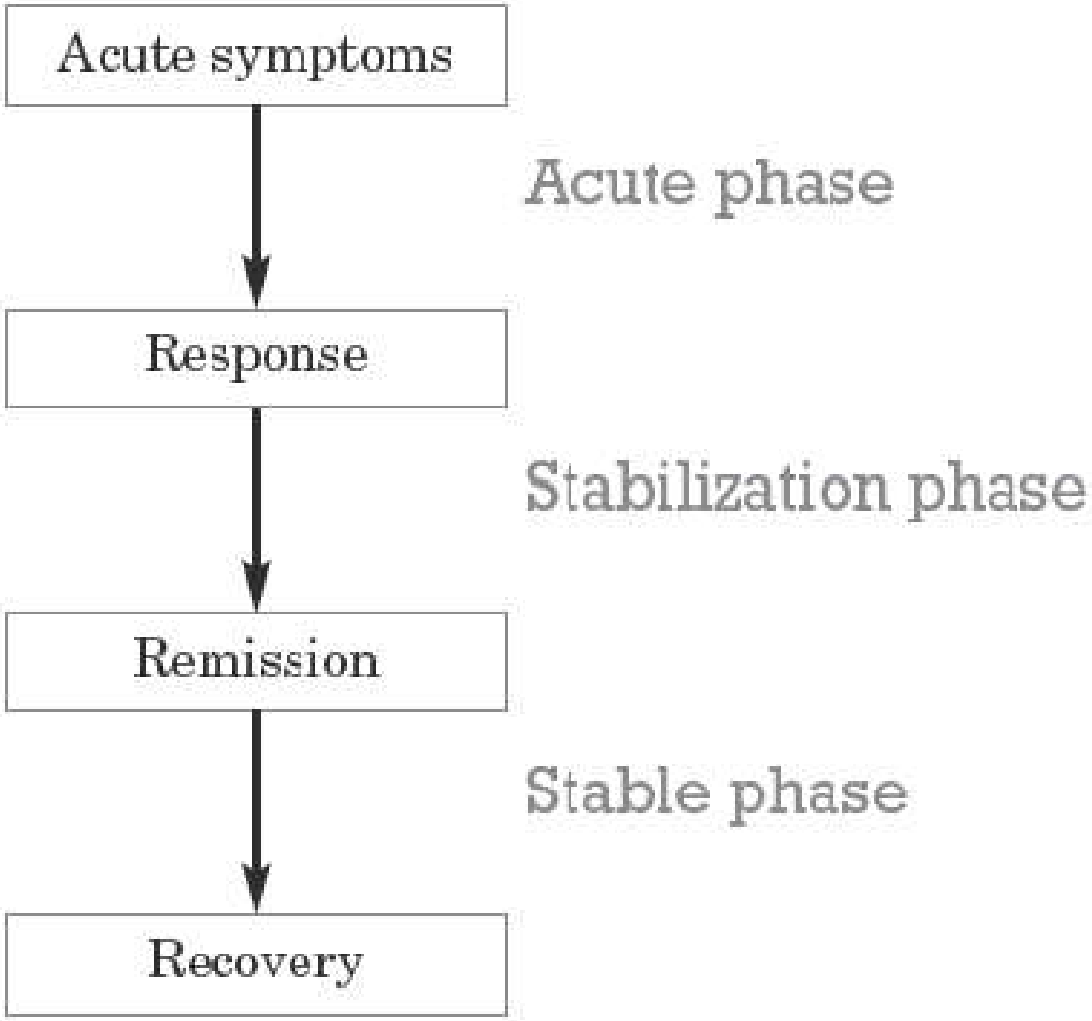
Adapted from Kinter et al. Int J Technol Assess Health Care 2009;25:35–41

Functional recovery as the most important outcome in schizophrenia



American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 4th edition, text revision. Washington DC: APA; 2000; Burns & Patrick. Acta Psychiatr Scand 2007;116:403–418

Figure 2. Stages in the recovery process



Tandon et al, 2006

Published in final edited form as:
Schizophr Res. 2011 October ; 132(1): 18–23. doi:10.1016/j.schres.2011.06.025.

Remission and Recovery during the First Outpatient Year of the Early Course of Schizophrenia

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Abstract

Background—Although in the early course of schizophrenia relapse prevention is of paramount importance, there is an increasing emphasis on establishing and maintaining sustained periods of symptom remission. Recovery in the early course of illness is also possible, although the rates of recovery are lower than for symptom remission. Symptom remission and recovery rates vary considerably across recent-onset schizophrenia studies because of lack of consistency in treatment interventions and in applying operational outcome criteria.

Method—Patients who were within two years of their first psychotic episode (N=77) who were treated with continuous antipsychotic medication in conjunction with psychosocial interventions (without targeted work rehabilitation) were assessed during the first outpatient year after hospital discharge. Published operational criteria were used to classify symptom remission and recovery.

Remission and Recovery during the First Outpatient Year of the Early Cours of Schizophrenia

RESULTS

- The rate of full symptom remission maintained for 6 months was 36%, while the rate of recovery for 6 months was 10%.
- When the same criteria were applied for a continuous period of one year, 22% of patients were found to achieve symptom remission but only 1% of patients met recovery criteria.
- Using multivariate prediction, the WAIS Comprehension score and **continuous pharmacological and psychosocial treatment** were significant predictors of 6 months good functional outcome.

Schizophr Res. 2011 October ; 132(1): 18–23. doi:10.1016/j.schres.2011.06.025.

Psychosocial tratments for Schizofrenia

EVIDENCE-BASED PRACTICES

1. ASSERTIVE COMMUNITY TREATMENT
2. FAMILY PSYCHOEDUCATION
3. SOCIAL SKILLS TRAINING
4. COGNITIVE BEHAVIOR THERAPY FOR PSYCHOSIS
5. SUPPORTED EMPLOYMENT
6. COGNITIVE REMEDIATION

Mueser K.T et al, Annu. Rev. Clin. Psychol. 2013. 9:465-97

Available online at www.sciencedirect.com
ScienceDirect
Schizophrenia Research 100 (2008) 108 – 119
SCHIZOPHRENIA RESEARCH
www.elsevier.com/locate/schres

Adjunctive psychosocial therapies for the treatment of schizophrenia

Thomas L. Patterson [a,*], Oscar R. Leeuwenkamp [b]

Abstract

Antipsychotic pharmacotherapy is the standard of care for the treatment of schizophrenia. Although pharmacotherapy effectively improves some symptoms, others can remain. Pharmacotherapy alone also tends to produce only limited improvement in social functioning and quality of life. Supportive psychosocial therapies have been used as adjuncts to pharmacotherapy to help alleviate residual symptoms and to improve social functioning and quality of life. Additionally, therapies with psychoeducational components can focus on improving medication adherence and reducing relapse and rehospitalization. This review describes the major psychosocial therapeutic strategies that have been used effectively in patients with schizophrenia (cognitive-behavioral therapy, family intervention, social skills, and cognitive remediation), with emphasis on their utility in improving medication adherence. Therapies that integrate various psychosocial therapeutic approaches are also discussed. It is concluded that psychosocial therapy is an effective adjunct to pharmacotherapy for schizophrenia. However, these therapies vary significantly in the functional domains that they address. It is therefore important to identify the form of psychosocial intervention most likely to benefit the individual patient, and to recognize that the effectiveness of any psychosocial intervention could be influenced by such factors as the presence and severity of psychotic or affective symptoms or cognitive impairment.

Adjunctive psychosocial therapies for the treatment of schizophrenia

Table 2
Domains of improvement with psychosocial therapies

Intervention	Domains most consistently improved	Domains less consistently improved
Cognitive-behavioral therapy (CBT)	Psychopathology, residual symptoms	Adherence, social function
Family intervention therapy (FIT)	Adherence, relapse, hospitalization, disease burden	Residual symptoms, social function
Social skills therapy (SST)	Social function, activities of daily life	Adherence, residual symptoms
Cognitive remediation therapy (CRT)	Cognitive function	Residual symptoms, social function
Integrated therapies	Social function, residual symptoms	Adherence, relapse

Schizophrenia Research 100 (2008) 108–119

Effect of Antipsychotic Medication Alone vs Combined With Psychosocial Intervention on Outcomes of Early-Stage Schizophrenia

A Randomized, 1-Year Study

Xiaofeng Guo, MD; Jinguo Zhai, MD; Zhening Liu, MD; Maosheng Fang, MD; Bo Wang, MD; Chuanyue Wang, MD; Bin Hu, MD; Xueli Sun, MD; Luxian Lv, MD; Zheng Lu, MD; Cui Ma, MD; Xiaolin He, MD; Tiansheng Guo, MD; Shiping Xie, MD; Renrong Wu, MD; Zhimin Xue, MD; Jindong Chen, MD; Elizabeth W. Twamley, PhD; Hua Jin, MD; Jingping Zhao, MD, PhD

Context: Antipsychotic drugs are limited in their ability to improve the overall outcome of schizophrenia. Adding psychosocial treatment may produce greater improvement in functional outcome than does medication treatment alone.

Objective: To evaluate the effectiveness of antipsychotic medication alone vs combined with psychosocial intervention on outcomes of early-stage schizophrenia.

Design: Randomized controlled trial.

Setting: Ten clinical sites in China.

Participants: Clinical sample of 1268 patients with early-stage schizophrenia treated from January 1, 2005, through October 31, 2007.

Intervention: Patients were randomly assigned to receive antipsychotic medication treatment only or antipsychotic medication plus 12 months of psychosocial intervention consisting of psychoeducation, family intervention, skills training, and cognitive behavior therapy administered during 48 group sessions.

Main Outcome Measures: The rate of treatment discontinuation or change due to any cause, relapse or remission, and assessments of insight, treatment adherence, quality of life, and social functioning.

Results: The rates of treatment discontinuation or change due to any cause were 32.8% in the combined treatment group and 46.8% in the medication-alone group. Comparisons with medication treatment alone showed lower risk of any-cause discontinuation with combined treatment (hazard ratio, 0.62; 95% confidence interval, 0.52-0.74; $P<.001$) and lower risk of relapse with combined treatment (0.57; 0.44-0.74; $P<.001$). The combined treatment group exhibited greater improvement in insight ($P<.001$), social functioning ($P=.002$), activities of daily living ($P<.001$), and 4 domains of quality of life as measured by the Medical Outcomes Study 36-Item Short Form Health Survey (all $P\leq.02$). Furthermore, a significantly higher proportion of patients receiving combined treatment obtained employment or accessed education ($P=.001$).

Conclusion: Compared with those receiving medication only, patients with early-stage schizophrenia receiving medication and psychosocial intervention have a lower rate of treatment discontinuation or change, a lower risk of relapse, and improved insight, quality of life, and social functioning.

Trial Registration: clinicaltrials.gov Identifier: NCT00654576

Arch Gen Psychiatry. 2010;67(9):895-904

Table 1. Content of Monthly Psychosocial Treatment Sessions

Month	Psychoeducation Topics	Family Intervention Topics	Skills Training Topics	Cognitive Behavior Therapy Topics
1	Introduction into program; discussion of goals and questions	Introduction into program; discussion of goals and questions	Medication management 1: identifying benefits of antipsychotic medication	Developing therapeutic alliance
2	What is schizophrenia?	Role of family in schizophrenia	Medication management 2: self-administration and evaluation of medication	Using the "ABC Model" to find connections between activating events, *b*eliefs, and *c*onsequences
3	Causal and triggering factors	Relatives sharing experiences of caring for patients	Medication management 3: adverse effects of antipsychotic medication	Intervening with auditory hallucinations (voices)
4	Description of various symptoms	Coping strategies: identifying, describing, clarifying, and teaching coping strategies used by families	Symptom management 1: identifying warning signs of relapse	Intervening with auditory hallucinations (voices)
5	Patients' concepts of illness and vulnerability-stress-coping model	Coping strategies: identifying, describing, clarifying, and teaching coping strategies used by families	Symptom management 2: developing relapse prevention plan	Intervening with delusions
6	Course and outcome	Helping families with problem solving	Verbal and nonverbal communication	Intervening with delusions
7	Treatment recommendations concerning pharmacotherapy	Helping families with problem solving.	Verbal and nonverbal communication	Intervening with anxiety, depression, and self-esteem issues
8	Risks associated with treatment withdrawal	Family communication	Learning and practicing problem-solving skills	Intervening with anxiety, depression, and self-esteem issues
9	Early detection of relapse	Family communication	Learning and practicing problem-solving skills	Relapse prevention
10	Pregnancy and genetic counseling	Behavior management	Job-finding skills	Relapse prevention
11	Discussion of open questions	Behavior management	Independent living skills	Enhancing medication adherence
12	Final session: review of content	Final session: review of content	Independent living skills	Enhancing medication adherence

Arch Gen Psychiatry. 2010;67(9):895-904

Table 3. Outcome Measures of Effectiveness in Patients Receiving Combined Treatment or Medication Treatment

Reason for Discontinuation of Treatment	No. (%)		Cox-Model Treatment Comparisons, HR (95% CI)	*P* Value
	Combined Treatment (n=604)	Medication Treatment (n=635)		
Any cause[a]	198 (32.8)	297 (46.8)	0.62 (0.52-0.74)	<.001
Any cause except change in medication or intolerability	176 (29.1)	269 (42.4)	0.57 (0.46-0.70)	<.001
Clinical relapse[b]	88 (14.6)	143 (22.5)	0.57 (0.44-0.74)	<.001
Lost to follow-up or patient's refusal	71 (11.8)	90 (14.2)	0.74 (0.54-1.01)	.05
Nonadherence	17 (2.8)	36 (5.7)	0.45 (0.25-0.79)	.006
Changing or stopping medication	17 (2.8)	19 (3.0)	0.84 (0.44-1.62)	.60
Intolerability	5 (0.8)	9 (1.4)	0.66 (0.22-1.99)	.46
Readmission	39 (6.5)	71 (11.2)	0.50 (0.34-0.74)	.007

Abbreviations: CI, confidence interval; HR, hazard ratio.
[a] Includes clinical relapse, lost to follow-up or patient's refusal, nonadherence, intolerability, and changing or stopping medication.
[b] Includes readmission.

Arch Gen Psychiatry. 2010;67(9):895-904

Integrating psychopharmacology and cognitive remediation to treat cognitive dysfunction in the psychotic disorders

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Cognitive deficits are a prominent and enduring aspect of schizophrenia, which pose a significant barrier to achieving functional goals. The most promising intervention for treating cognitive impairment is cognitive remediation (CR), a behaviorally based therapy associated with medium effect sizes for cognitive and functional outcomes. However, there is a sizeable group of nonresponders whose CR outcomes become limited when the therapeutic approach fails to address individual differences in baseline cognition, motivation variables, and the extent to which CR offers opportunities for generalization. This speaks to a need to develop cognitive interventions that are both personalized and scalable. Emerging data suggest that specific pharmacological agents have the potential to enhance and accelerate behaviorally based CR effects. This article will review the rationale and preliminary evidence to support combining CR and pharmacotherapy. We will review crucial aspects of cognitive interventions that offer the most promise for improving not only cognitive outcomes, but also for enhancing improvement in real-world functioning. Finally, we will address methodological issues to be considered for future research on combined pharmacological and CR interventions.

Received 29 May 2013; Accepted 15 June 2013

Key words: Cognition, psychosis, cognitive remediation, cognitive enhancers.

doi:10.1017/S1092852913000461

Can functional recovery be achieved using integrated treatment?

1-year follow-up of first-episode patients without prior treatment:

- Integrated care (n=39) including pharmacotherapy, psychosocial treatment and psychoeducation
- Medication only (n=34)

	Integrated care (%)	Medication only (%)	p value
Relapse	10.3	35.7	<0.01
Rehospitalization	5.1	10.7	NR
Adherence	85	67.6	<0.01
Symptomatic remission	94.9	58.8	NR
Functional remission	56.4	3.6	<0.01
Functional recovery	56.4	2.9	<0.01

Integrated care provided additional benefits compared with medication alone

NR, not reported

Valencia et al. Schizophr Res Treatment 2012, May 10 [Epub ahead of print]

Schizophr Bull. 2015 Sep;41(5):1192-203. doi: 10.1093/schbul/sbv058. Epub 2015 May 20.

Feasibility and Effectiveness of a Multi-Element Psychosocial Intervention for First-Episode Psychosis: Results From the Cluster-Randomized Controlled GET UP PIANO Trial in a Catchment Area of 10 Million Inhabitants.

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Author information

Abstract

Integrated multi-element psychosocial interventions have been suggested to improve the outcomes of first-episode psychosis (FEP) patients, but they have been studied primarily in experimental settings and in nonepidemiologically representative samples. Thus, we performed a cluster-randomized controlled trial, comparing an integrated multi-element psychosocial intervention, comprising cognitive behavioral therapy, family intervention, and case management, with treatment as usual (TAU) for FEP patients in 117 community mental health centers (CMHCs) in a large area of northern Italy (10 million inhabitants). The randomized units (clusters) were the CMHCs, and the units of observation the patients (and, when available, their family members). The primary hypotheses were that add-on multicomponent intervention: (1) results in greater improvements in symptoms, as assessed with positive and negative syndrome scale and (2) reduces in-hospital stay, based on days of hospitalization over the 9-month follow-up. Four hundred and forty-four FEP patients received the intervention or TAU and were assessed at baseline and 9 months. Based on the retention rates of patients (and families) in the experimental arm, multi-element psychosocial interventions can be implemented in routine mental health services. Regarding primary outcomes, patients in the experimental arm showed greater reductions in overall symptom severity, while no difference could be found for days of hospitalization. Among the secondary outcomes, greater improvements were detected in the experimental arm for global functioning, emotional well-being, and subjective burden of delusions. No difference could be found for service disengagement and subjective burden of auditory hallucinations. These findings support feasibility and effectiveness of early interventions for psychosis in generalist mental health services.

Feasibility and Effectiveness of a Multi-Element Psychosocial Intervention for First-Episode Psychosis: Results From the Cluster-Randomized Controlled GET UP PIANO Trial in a Catchment Area of 10 Million Inhabitants.

Table 3. Nonspecific Interventions, Admissions, and Service Disengagement During the Period Between Baseline (BL) (After Clinical Stabilization) and 9-Month Follow-Up (FU)

	Period Between BL and FU		
	Treatment as Usual Group (n = 172)	Experimental Treatment Group (n = 272)	Test and Significance of Difference
Nonspecific interventions			
Patients receiving nonspecific interventions, n (%)	66 (49.3%) (38 missing)	68 (27.3%) (23 missing)	$\chi^2 = 18.44$, $df = 1$, $P < .001$
Families receiving nonspecific interventions, n (%)	34 (25.4%) (38 missing)	25 (10.0%) (23 missing)	$\chi^2 = 15.72$, $df = 1$, $P < .001$
Hospital admissions			
At least 1 admission, n (%)	26 (15.8%) (7 missing)	45 (16.9%) (5 missing)	$\chi^2 = 0.09$, $df = 1$, $P = .765$
Number of admissions (for admitted pts), n (%)			
1	18 (69.2%)	31 (68.9%)	$\chi^2 = 0.001$, $df = 1$, $P = .976$
>1	8 (30.8%)	14 (31.1%)	
Mean length of stay (days) (for admitted pts), mean (SD) [range]	23.5 (19.6) [5–75] (2 missing)	20.8 (16.0) [4–82][a] (3 missing)	$t = .61$, $df = 64$, $P = .546$
Service disengagement			
In contact with service at FU n (%)	157 (91.3%)	247 (90.8%)	$\chi^2 = 0.03$, $df = 1$, $P = .866$
Reasons for treatment discontinuation (for disengaged pts), n (%)			
Appropriate termination	4 (26.7%)	4 (16.0%)	na
Drop out	11 (73.3%)	21 (84.0%)	
Dissatisfaction with the care received	0 (0.0%)	1 (4.7%)	
Self-perceived clinical improvement	5 (45.4%)	6 (28.6%)	
Practical constraints	0 (0.0%)	2 (9.5%)	
Other reasons	1 (9.2%)	6 (28.6%)	
No answer	5 (45.4%)	6 (28.6%)	
Months from BL to the last contact (for disengaged pts), mean (SD)	4.6 (2.2) (1 missing)	3.3 (3.1) (1 missing)	$t = 1.38$, $df = 36$, $P = .177$

Note: na, not applicable. Due to the low number of subjects, only descriptives are allowed.
[a]1 outlier (with 1 admission of 244 days) was deleted from the calculation of the days of admission.

Feasibility and Effectiveness of a Multi-Element Psychosocial Intervention for First-Episode Psychosis: Results From the Cluster-Randomized Controlled GET UP PIANO Trial in a Catchment Area of 10 Million Inhabitants.

Table 4. Primary and Secondary Outcomes: PANSS, PSYRATS, GAF, and HAMILTON of Intention to Treat Patients Assessed at Baseline (BL) (After Clinical Stabilization) and at 9-Month Follow-Up (FU). Total Number of Days of Hospitalization During the Period Between Baseline (After Clinical Stabilization) and 9-Month Follow-Up, Together With Weighted Regression Coefficients of Experimental Treatment vs Treatment as Usual (95% CI) and Effect Sizes (95% CI)

	Treatment as Usual Group		Experimental Treatment Group				
Primary Outcomes	BL (n = 172)	FU (n = 153)	BL (n = 272)	FU (n = 239)	Weighted Regression Coefficient[#] of Experimental Treatment vs Treatment as Usual (95% CI)	P-Value	Effect Size[*] (95% CI)
PANSS total	2.32 (0.68)	1.78 (0.64)	(1 missing) 2.37 (0.67)	(1 missing) 1.67 (0.57)	−0.11 (−0.22 to −0.01)	.044	−0.24 (−0.47 to −0.01)
PANSS positive	2.22 (0.86)	1.52 (0.70)	(2 missing) 2.30 (0.88)	(2 missing) 1.46 (0.57)	−0.07 (−0.18 to 0.04)	.232	−0.15 (−0.36 to 0.07)
PANSS negative	2.56 (1.11)	(4 missing) 2.01 (0.99)	(3 missing) 2.51 (1.14)	(2 missing) 1.87 (0.94)	−0.12 (−0.29 to 0.04)	.149	−0.17 (−0.37 to 0.03)
PANSS general	2.27 (0.67)	1.81 (0.64)	(1 missing) 2.35 (0.65)	(3 missing) 1.68 (0.56)	−0.14 (−0.25 to −0.03)	.015	−0.29 (−0.52 to −0.06)
Hospital admissions	Period between BL and FU (n = 163)		Period between BL and FU (n = 264)				
Total number of days of hospitalization mean (SD) [median; range]	5.4 (20.2) [0; 0−150]		4.6 (15.2) [0; 0−150][§]		−0.88 (−4.05, 2.29)	.586	−0.08 (−0.33 to 0.18)

	Treatment as Usual Group		Experimental Treatment Group				
Secondary Outcomes	BL (n = 172)	FU (n = 153)	BL (n = 272)	FU (n = 239)	Weighted Regression Coefficient[#] of Experimental Treatment vs Treatment as Usual (95% CI)	P-Value	Effect Size[*] (95% CI)
GAF score	(1 missing) 45.69 (12.96)	(1 missing) 60.11 (16.63)	(1 missing) 44.46 (13.81)	63.15 (16.94)	3.98 (1.15 to 6.82)	.006	0.35 (0.06 to 0.64)
HAMILTON score	(2 missing) 16.42 (9.90)	(5 missing) 10.62 (10.17)	(1 missing) 17.29 (8.29)	(3 missing) 8.81 (6.58)	−1.86 (−3.40 to −0.31)	.019	−0.25 (−0.48 to −0.03)
PSYRAT auditory hallucination scale	N = 22[a] 2.03 (1.25)	N = 22 0.51 (1.08)	N = 29[b] 1.67 (1.34)	N = 29 0.41 (0.93)	−0.17 (−0.75 to 0.42)[^]	.580	−0.23 (−1.13 to 0.66)
PSY AHS distress	2.13 (1.52)	0.76 (1.48)	1.69 (1.57)	0.48 (1.09)	−0.40 (−1.21 to 0.40)[^]	.328	−0.62 (−1.85 to 0.62)
PSY AHS cognitive	2.38 (1.39)	0.57 (1.08)	1.94 (1.48)	0.42 (0.90)	−0.25 (−0.90 to 0.39)[^]	.443	−0.35 (−1.29 to 0.60)
PSY AHS physical	1.87 (1.19)	0.45 (0.97)	1.56 (1.27)	0.40 (0.94)	−0.09 (−0.61 to 0.45)[^]	.772	−0.07 (−0.82 to 0.68)
PSYRAT delusion scale	N = 31[c] 2.78 (1.15)	N = 31 1.59 (1.38)	N = 50[d] 3.12 (0.73)	N = 50 0.76 (1.11)	−0.96 (−1.52 to −0.39)[^]	.001	−0.82 (−1.29 to −0.35)
PSY DS distress	2.62 (1.38)	1.60 (1.53)	3.05 (0.97)	0.75 (1.12)	−0.93 (−1.59 to −0.28)[^]	.005	−0.78 (−1.32 to −0.23)
PSY DS cognitive	2.84 (1.14)	1.65 (1.45)	3.15 (0.77)	0.77 (1.12)	−1.01 (−1.56 to −0.46)[^]	.000	−0.86 (−1.32 to −0.39)

Integrated care in patients with schizophrenia: results of trials published between 2011 and 2013 focusing on effectiveness and efficiency

Daniel Schöttle[a], *Anne Karow*[a], *Benno G. Schimmelmann*[b], *and Martin Lambert*[a]

Purpose of review

Overview on integrated care trials focusing on effectiveness and efficiency published from 2011 to 2013.

Recent findings

Eight randomized controlled trials (RCTs) and 21 non-RCT studies were published from 2011 to 2013. Studies differed in several methodological aspects such as study population, psychotherapeutic approaches used, outcome parameters, follow-up times, fidelities, and implementation of the integrated care model and the nation-specific healthcare context with different control conditions. This makes it difficult to draw firm conclusions. Most studies demonstrated relevant improvements regarding symptoms ($P=0.001$) and functioning ($P=0.01$), quality of life ($P=0.01$), adherence ($P<0.05$) and patient's satisfaction ($P=0.01$), and reduction of caregiver's stress ($P<0.05$). Mean total costs were favoring or at least equalizing costs but with positive effects found on subjective health favoring integrated care models.

Summary

There is an increasing interest in the effectiveness and efficiency of integrated care models in patients with mental disorders, specifically in those with severe and persistent mental illness. To increase generalizability, future trials should exactly describe rationales and content of integrated care model and control conditions.

Curr Opin Psychiatry 2013, 26:384–408

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KEY POINTS

- Integrated care can be defined as a patient-centred innovative care model in which multidisciplinary and multisite pathways are linked and coordinated, and evidence-based treatments are delivered with a focus on continuity of care.
- Most RCTs and non-RCTs show an advantage of the integrated care model compared with treatment-as-usual with regard to effectiveness and efficiency in the treatment of schizophrenia.
- Further studies should answer the question of whether integrated care should be an 'open-end' intervention and exactly which pharmacological and psychosocial interventions in specific patient groups improve outcome within integrated care models; they should also assess cost-effectiveness.
- Independently of the integrated care model chosen, there are several core features which need to be implemented.

Different integrated care models use different intensive care approaches, such as 'Community Mental Health Teams' (CMHTs), Intensive Case Management (ICM), or Assertive Community Treatment (ACT). Most of them have been proven to be effective interventions in treating people with severe and persistent mental disorders (SPMI)

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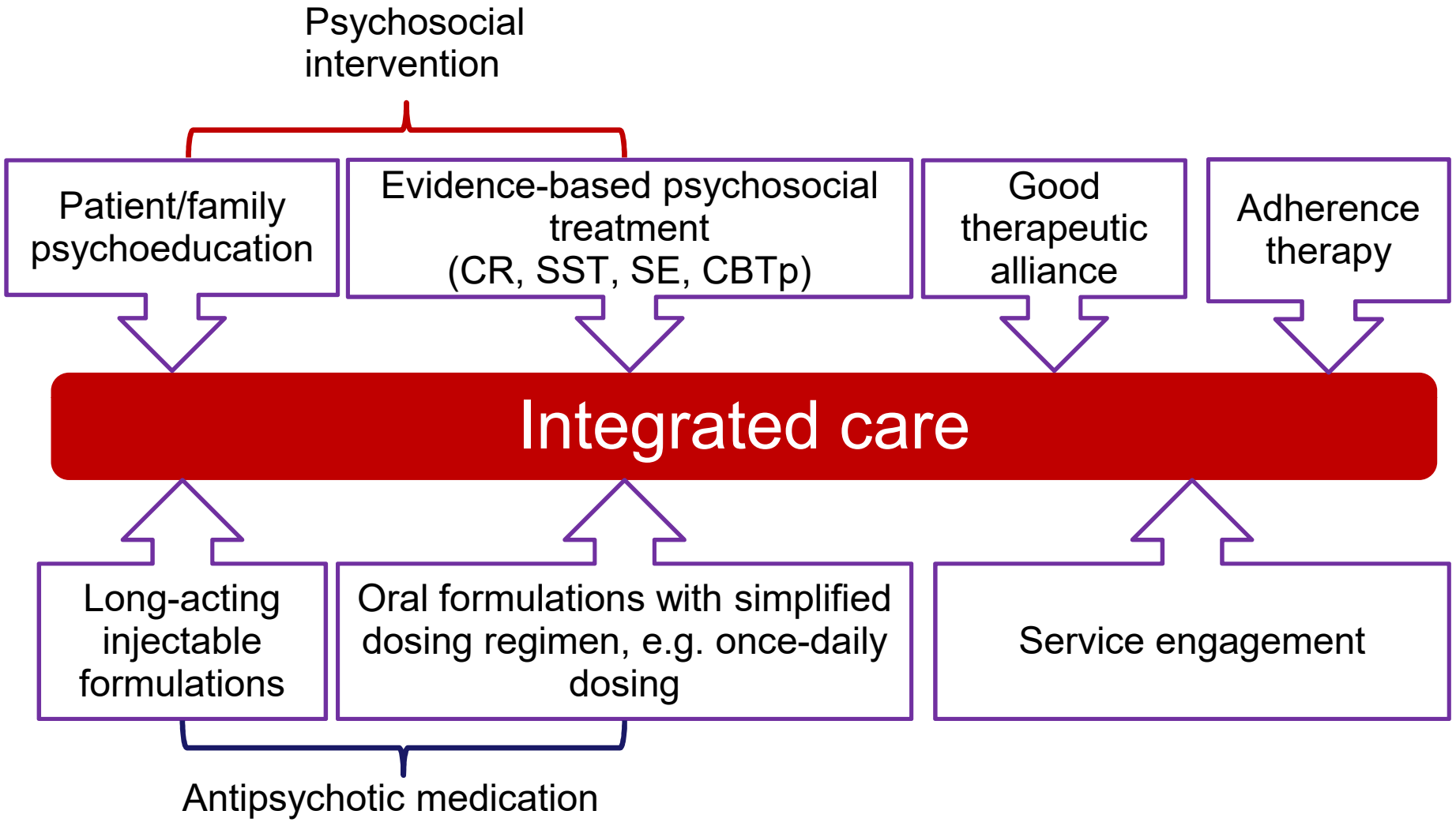
Components for successful treatment



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