When medication is NOT enough for psychosis

Evidence-based approaches to fill the gaps

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Potential conflicts of interest

Boehringer-Ingleheim: Consultant

Janssen: Advisory Board, Consultant, Speaker

Signant Health: Consultant, Speaker

Otsuka Pharmaceuticals: Consultant Speaker

Merck: Advisory Board

When medication is not enough

- Experiences of those with psychosis
- The role of Medication
- Psychosocial Treatments
  - CBT for psychosis
  - CAT for bypassing cognitive difficulties
  - MOVE for negative symptoms
  - Many other evidence-supported options

Schizophrenia:
Signs and symptoms related to outcome

Positive Symptoms
Delusions
Hallucinations
Disorganized speech/behavior

← Medications Primarily Address

Negative Symptoms
Affective Blunting
Poverty of speech
Amotivation
Decreased activity
Social withdrawal

Community Functioning/Behavior
Work/School
Interpersonal relationships
Self-care/ADLs
Medication Adherence

Cognitive Difficulties
Attention
Memory
Executive functions
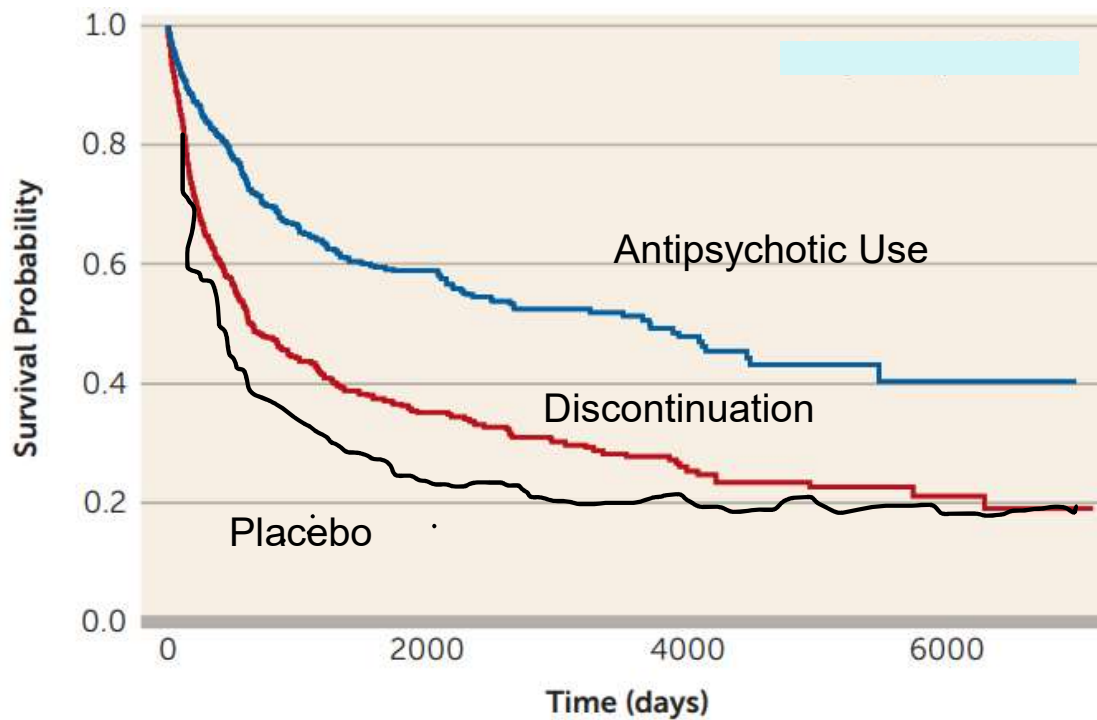Social Cognition

Comorbid Conditions
Mood
Substance abuse
Anxiety

What is the role of medication?

Artist rendering: Time to Relapse without antipsychotic medication –

The survival curves look very similar in many studies

Baldessarini RJ, et al. Tardive Dyskinesia: APA Task Force Report 18, 1980

Tihonen et al Am J Psychiatry 2018; 175:765–773; doi: 10.1176/appi.ajp.2018.17091001

Only 50% of medications prescribed are taken

True in medicine in general

Adherence has been referred to as America's other drug problem (US Surgeon General).

A gap in having antipsychotic medication available as short as 11 days doubles the risk of hospitalization in schizophrenia.

On average an individual will have 8-9 relapses in a 5-year period

Medication follow-through is arguably one of the most modifiable obstacles to clinical stability and relapse prevention

Medications have side effects. Often intolerable.

Medication often treats positive symptoms incompletely

Medication does not address many of the other symptom types.

Farley et al., Prim Care Companion CNS Disord. 2012; 14(3): PCC.11m01324; Lacro JP, et al. J Clin Psychiatry. 2002;63:892-09)

Emsley et al. BMC Psychiatry 2013, 13:50; Law MR et al. J Clin Psychiatry. 2008;69(1):47-53. Kisimoto et al., Schiz Bul 2018; 44; 603-619

CBT for Persistent Positive Symptoms

Many individuals treated with antipsychotic medications continue to experience delusions and/or hallucinations.

These persisting positive symptoms can be extremely distressing and negatively impact daily functioning.

It is important to reduce persistent symptoms and the distress and problems with functioning associated with them.

Sensky et al., 2000; Kane & Marder, 1993; Pantelis & Barnes, 1996;Wiersma et al., 1998; O'Connor & Herman, 1993; Cather et al., 2004

Cognitive Behavior Therapy for Psychosis:

Goals of Treatment and Description

CBT is focused on helping the individual to develop alternative explanations for the symptoms of their illness, and to reduce the impact of these symptoms on their behavior.

In addition, focus is on changing underlying views and beliefs about self and/or others

Turkington et al., 2006; Tarrier & Wykes, 2004; Kuipers et al., 2006; van der Gaag 2006; Velligan et al.; 2015 May;41(3):597-603. doi: 10.1093/schbul/sbu127. Epub 2014 S

Information Processing: Reasoning and Appraisal Biases

We know that in depression, a person may have a negative view of themselves, of others and of their future. They tend to see the world through this distorted point of view and interpret events in a manner consistent with this view.

Similarly, a person with psychosis can develop a schema or world view that will predispose them to paranoia or other types of delusional thinking should they become psychotic.

Information is then interpreted in light of these pre-existing models. Confirmatory evidence is weighted more heavily.

Important to Normalize

Everybody believes something that other people don't (look at politics right now). This is a normal phenomenon.

According to a 2006 Gallop Poll **75%** of Americans believe in one or more of the following: Witches, ESP, supernatural powers, ghosts, clairvoyance, astronomy.

Many famous people have heard voices—people can have productive and even extraordinary lives while having symptoms
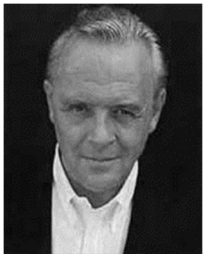
Skills for Coping with Hallucinatory Experiences and Acceptance

Distraction

Focusing

Listen for positive voices; talk back, negotiate

Voicehearers.org

Addressing Distressing or Problematic Beliefs

Individuals are used to having to defend their ideas and to being patronized.

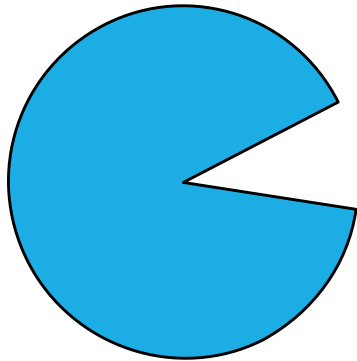Confronting causes individuals to have greater conviction.

It is equally important not to agree.

This fine line means that the therapist must be very careful in choosing his/her words, remaining interested and attempting to understand. Allow genuine confusion to work.

Investigate evidence using the internet and other sources (e.g. costs and of 24-hour surveillance, voodoo, listening devices, stigmata)

Turkington et al., 2006; Tarrier & Wykes, 2004; Kuipers et al., 2006; van der Gaag 2006; Velligan et al.; 2015 May;41(3):597-603. doi: 10.1093/schbul/sbu127. Epub 2014 Sep 5

Pie Charts and Delusional Conviction:
Coughing means there is a conspiracy against me

10% Believe there may be another explanation
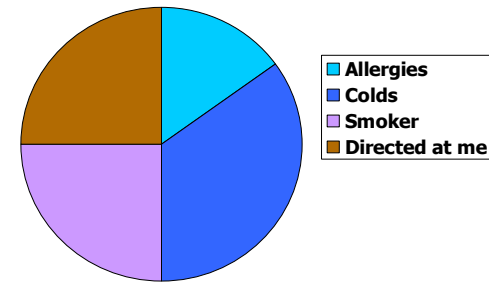
90% Convinced that a spell has been placed on me

■	Allergies
■	Colds
■	Smoker
■	Directed at me

Testing out beliefs

"Everyone on the bus wants to kill me."

Testing out beliefs

"Some people on the bus are ok."

Effect Sizes from CBTp studies (post-treatment CBTp/control);

CBT is recommended in PORT Schizophrenia Guidelines and by the NHS in the UK
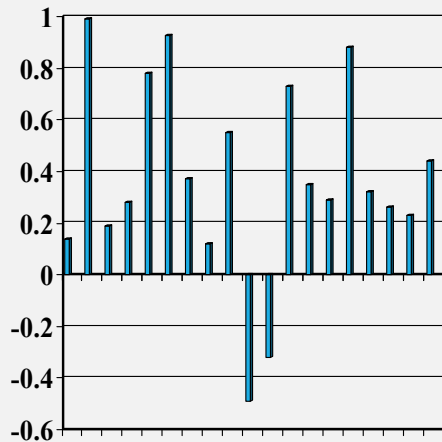
- Data available from 19 studies.
- Mean ES =0.37 (sd=0.39, median=0.32, range -0.49 to 0.99).
- 74% achieved at least a small ES,
- 32% a least a moderate ES,
- 16% a large ES

Wykes et al. Am J Psychiatry 2011; 168:472–485)

Beyond Positive Symptoms

- Cognition
- Motivation
- Functioning
- Recovery

Neuropsychological Profile for Individuals with Schizophrenia
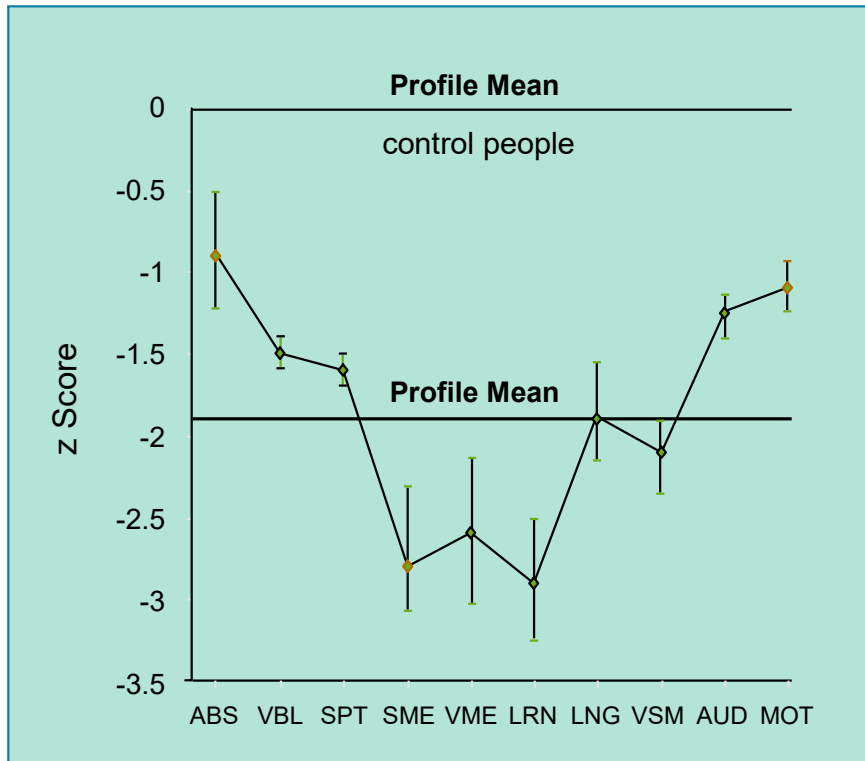
ABS – Abstraction
VBL – Verbal Cognitive
SPT – Spatial Organization
SME – Semantic Memory
VME – Visual Memory
LRN – Verbal Learning
LNG – Language
VSM – Visual-Motor Processing and Attention
AUD – Auditory Processing and Attention
MOT – Motor Speed and Sequencing

Specific Neurocognitive Difficulties

ATTENTION   **MEMORY**   **INFORMATION-PROCESSING SPEED**   **EXECUTIVE FUNCTIONS**
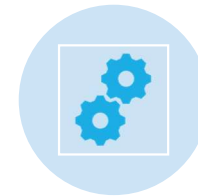
Stable over time

Often present before the onset of psychotic symptoms

Gold JM and Harvey PD Psychiatr Clin North Am, 1993; 16: 295-312

Difficulties in Social Cognition
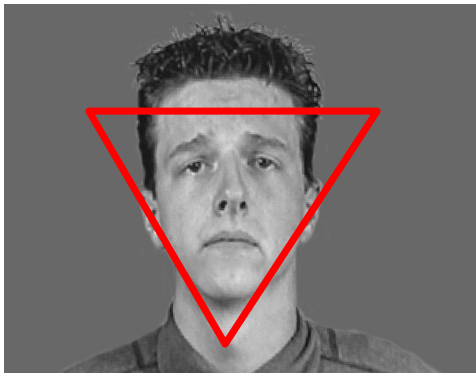
Social Cognition:

the ability to

       perceive,

       interpret and

       respond to others

mediates the relationship between non social cognition (e.g. memory, attention, information processing speed) and functional outcomes in the social realm.

emotional processing-the ability to make good guesses about the emotional states of others evident in facial expression and voice tone

Roberts, D. L., & Penn, D. L. (2009). Social cognition and interaction training (SCIT) for outpatients with schizophrenia: a preliminary study. *Psychiatry research*, *166*(2-3), 141–147. https://doi.org/10.1016/j.psychres.2008.02.007

Cognitive difficulties predict important aspects of functional outcome

Executive Function		ADL's
Attention	→	Social Function
Memory		Work
Psychomotor Speed		
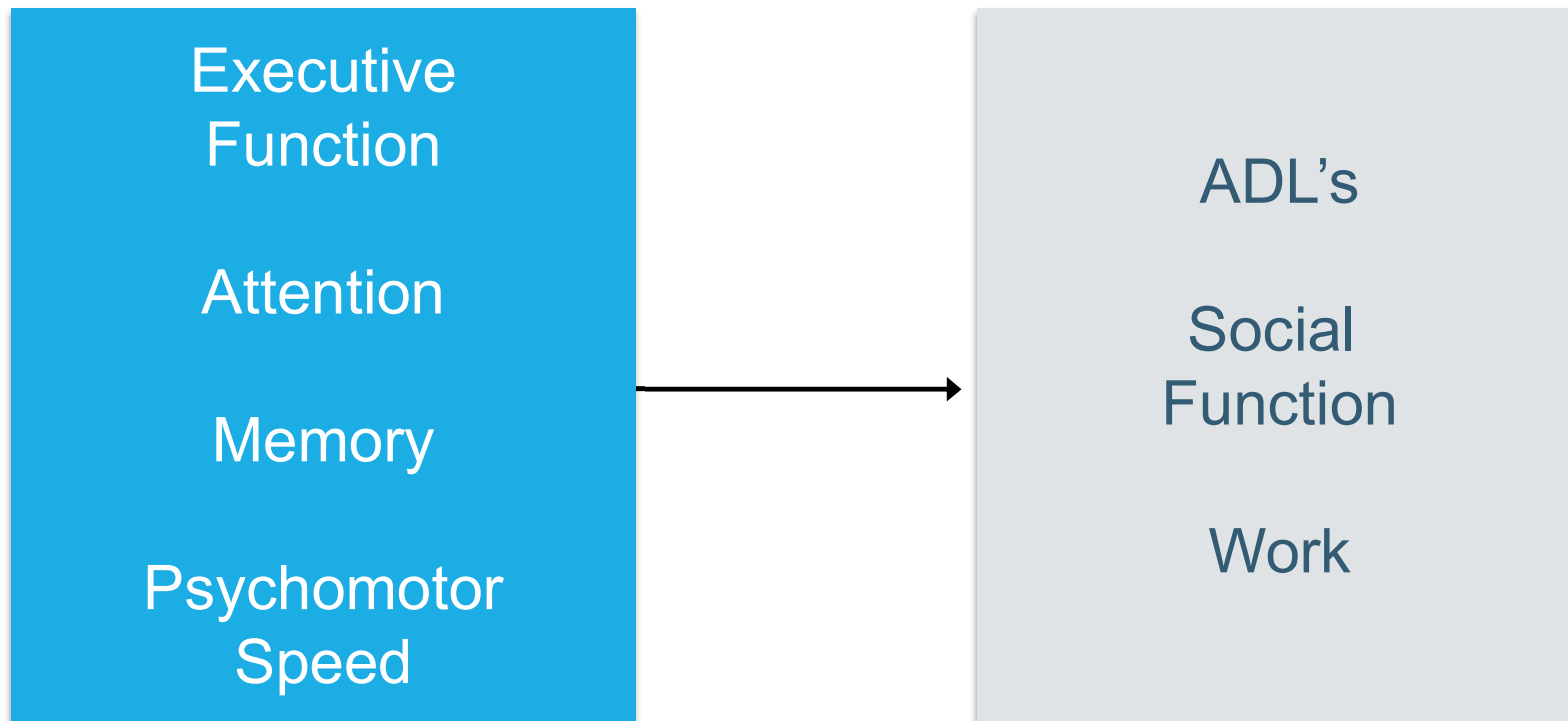
Green MF. Am J Psychiatry, 1996; 153: 321-330;Velligan et al., Schiz Res, 1997; 25: 21-31

Interventions for Cognitive Difficulties

Cognitive Remediation

- Improves cognitive functioning (small but significant and reproducible effects overall)
- Not well integrated into clinical treatment
- Works best as part of a multimodal program
- A number of programs specifically address social cognition

Compensatory strategies/environmental supports

- Designed to bypass difficulties

Bowie et al., Schizophrenia ResearchVolume 215, January 2020, Pages 49-53; Roberts, D. L., & Penn, D. L. (2009). Social cognition and interaction training (SCIT) for outpatients with schizophrenia: a preliminary study. *Psychiatry research*, *166*(2-3), 141–147. https://doi.org/10.1016/j.psychres.2008.02.007

Compensatory strategies can reduce the functional consequences of cognitive difficulties

Maples, N. J., & Velligan, D. I. (2008). *American Journal of Psychiatric Rehabilitation, 11*(2), 164–180. https://doi.org/10.1080/15487760801963686
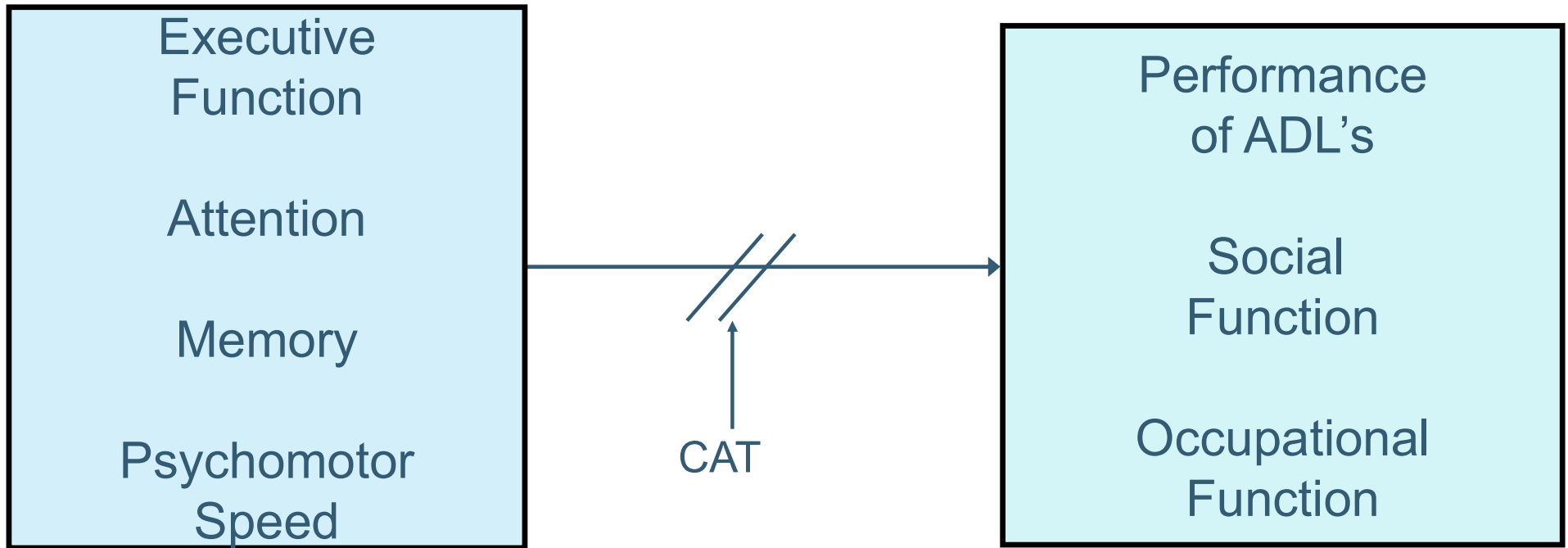
How CAT relies on automatic processes

- Environmental cues get us ready to act

- Cues are easier to follow than to resist

- Cues increase the experience of fluency by making the behavior "feel" easy to do, familiar, and true

- Reorganization of belongings decreases number of steps required, thus increasing the experience of fluency

- Repetition with verbal or visual cues increases familiarity and the sense of "truth"

- Repetition of behavior leads to habit formation, automaticity

Prior to intervention—Dresser and Drawers

Maples, N. J., & Velligan, D. I. (2008). *American Journal of Psychiatric Rehabilitation, 11*(2), 164–180. https://doi.org/10.1080/15487760801963686

CAT Intervention for Dressing

Apathy   Disinhibition   Mixed

Maples, N. J., & Velligan, D. I. (2008). *American Journal of Psychiatric Rehabilitation, 11*(2), 164–180. https://doi.org/10.1080/15487760801963686

Problems with Memory and Organization

Did I take my medication today?

Imrpoving Medication Follow Through

Maples, N. J., & Velligan, D. I. (2008). *American Journal of Psychiatric Rehabilitation, 11*(2), 164–180. https://doi.org/10.1080/15487760801963686

Checklists for everyday behaviors

- Take AM Medication
- Take shower
- Use Deodorant
- Call Susan
- Make a time to see Frank
- Play guitar
- Walk in the park

Daily Schedule

	Mon	Tues	Wed	Thurs	Fri	Sat	Sun
8							
9							
10							
11							
12							
1							
2							
3							
4							
5							
6							

Velligan et al., Schizophrenia Bulletin 2009;35(1S):345-346.;
Maples & Velligan Am J Psychiatric Rehab 2008 Apr;11(2):164-180

Dental Hygiene

Brush Teeth Everyday

Maples, N. J., & Velligan, D. I. (2008). *American Journal of Psychiatric Rehabilitation, 11*(2), 164–180. https://doi.org/10.1080/15487760801963686

Prior to Intervention

After to Intervention

Cleaning Supplies

Maples, N. J., & Velligan, D. I. (2008). *American Journal of Psychiatric Rehabilitation, 11*(2), 164–180. https://doi.org/10.1080/15487760801963686
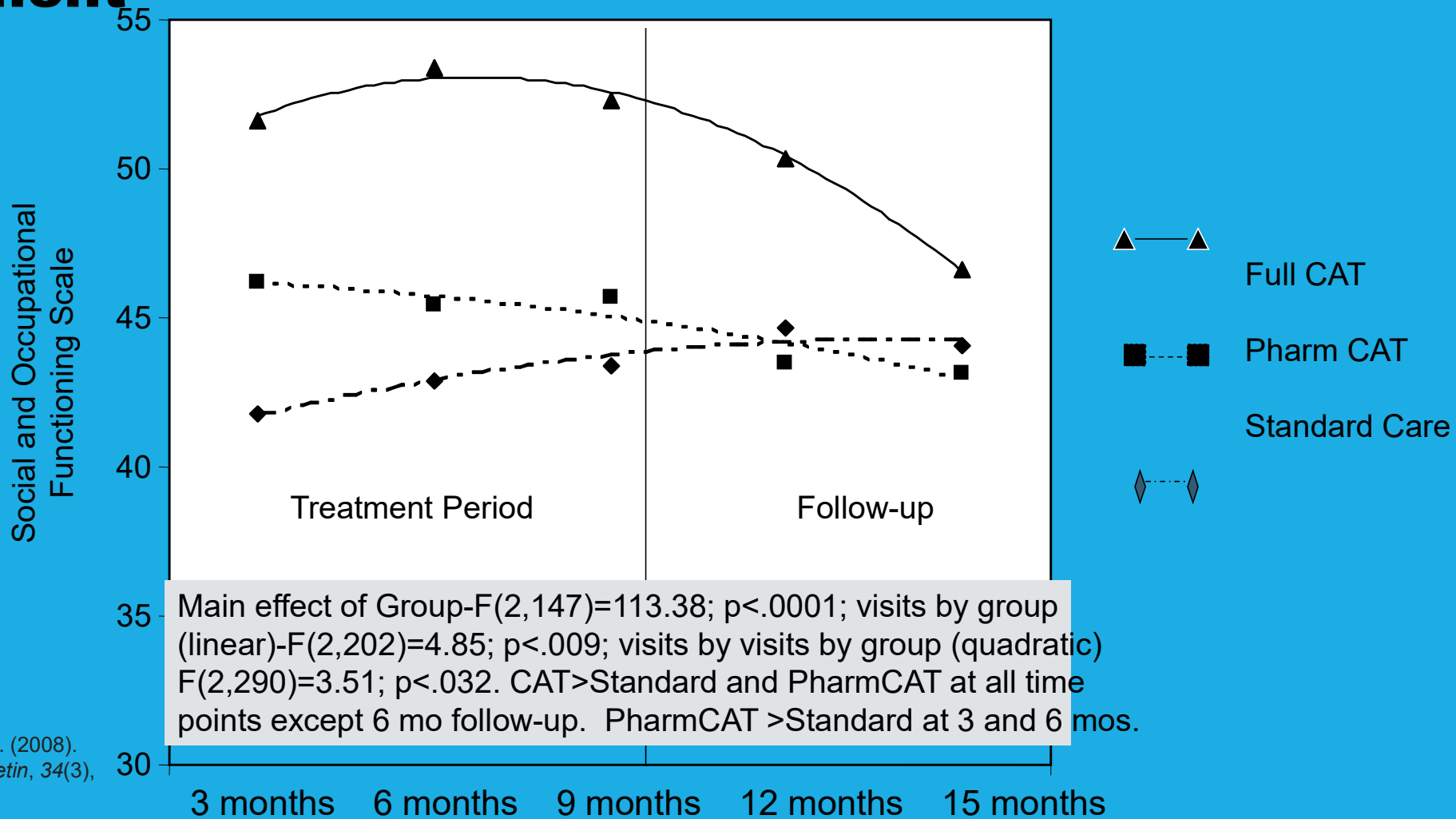
Medication Adherence Over Time by Treatment
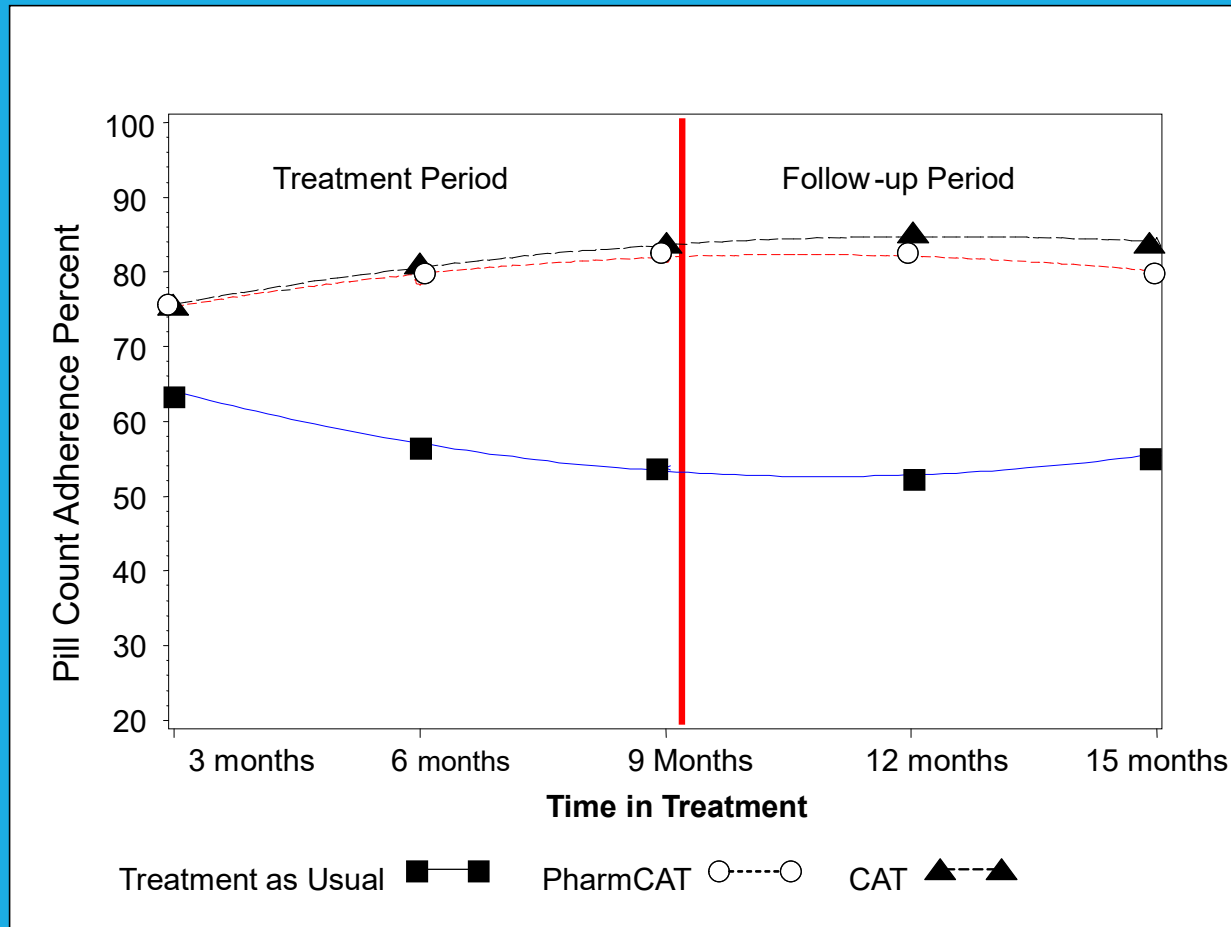
Similar results with pharmacy records

Main effect of group- $F_{(2,138)}=23.51$; $p<.0001$; visits by group (linear)- $F_{(2,264)}=2.85$; $p<.06$; visits by visits by group (quadratic)- $F_{(2,251)}=3.46p$ $p<.033$.

Velligan, D. I., et al. (2008). *Schizophrenia bulletin*, *34*(3), 483–493.

Social and Occupational Functioning Over Time by Treatment

Social and Occupational Functioning Scale (y-axis: 30 to 55)

Treatment Period | Follow-up

Legend:
- Full CAT (triangle, solid line)
- Pharm CAT (square, dotted line)
- Standard Care (diamond, dash-dot line)

x-axis: 3 months, 6 months, 9 months, 12 months, 15 months

Main effect of Group-$F_{(2,147)}$=113.38; p<.0001; visits by group (linear)-$F_{(2,202)}$=4.85; p<.009; visits by visits by group (quadratic) $F_{(2,290)}$=3.51; p<.032. CAT>Standard and PharmCAT at all time points except 6 mo follow-up. PharmCAT >Standard at 3 and 6 mos.

Velligan, D. I., et al. (2008). *Schizophrenia bulletin*, *34*(3), 483–493.

Time to Relapse by Treatment Group

PharmCAT

CAT

Standard

Survival Distribution Function

Time in Months

Velligan, D. I., et al (2008). *Schizophrenia bulletin*, *34*(3), 483–493.
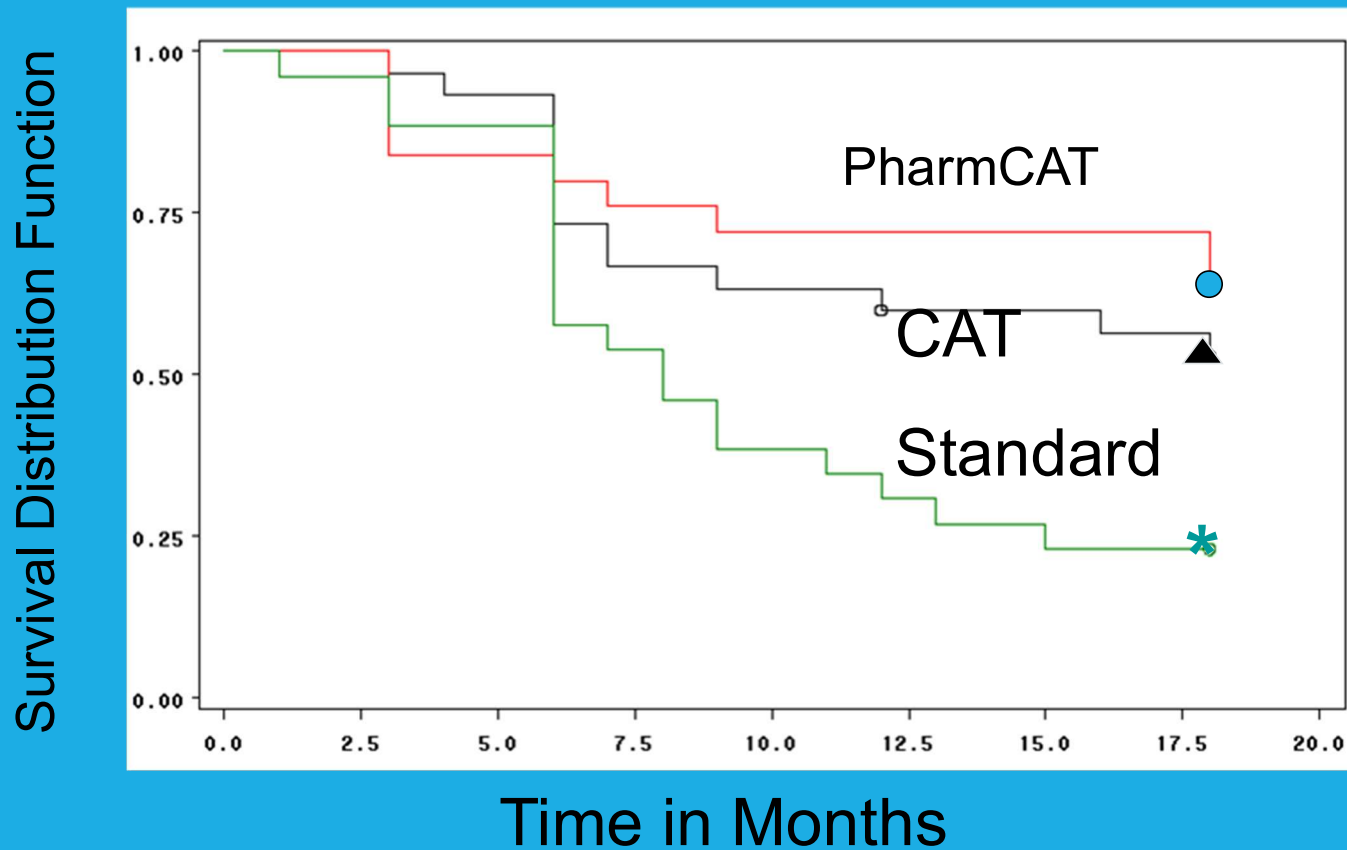
What about persistent negative symptoms?

What are negative symptoms?

- Negative symptoms are defined as the absence or reduction of behaviors that are normally present in the general population

- This is in contrast to positive symptoms which are behaviors that are normally absent in the general population

Alphs & Sommerfelt, 1989

Domains of Negative Symptoms

Anhedonia
Inability to feel pleasure-manifested in decreased frequency of participation in pleasurable activities, decreased feelings of pleasure when either anticipating or experiencing these activities

Asociality
Lack of desire to participate and actual participation in social activities, Lack of engagement with others

Avolition
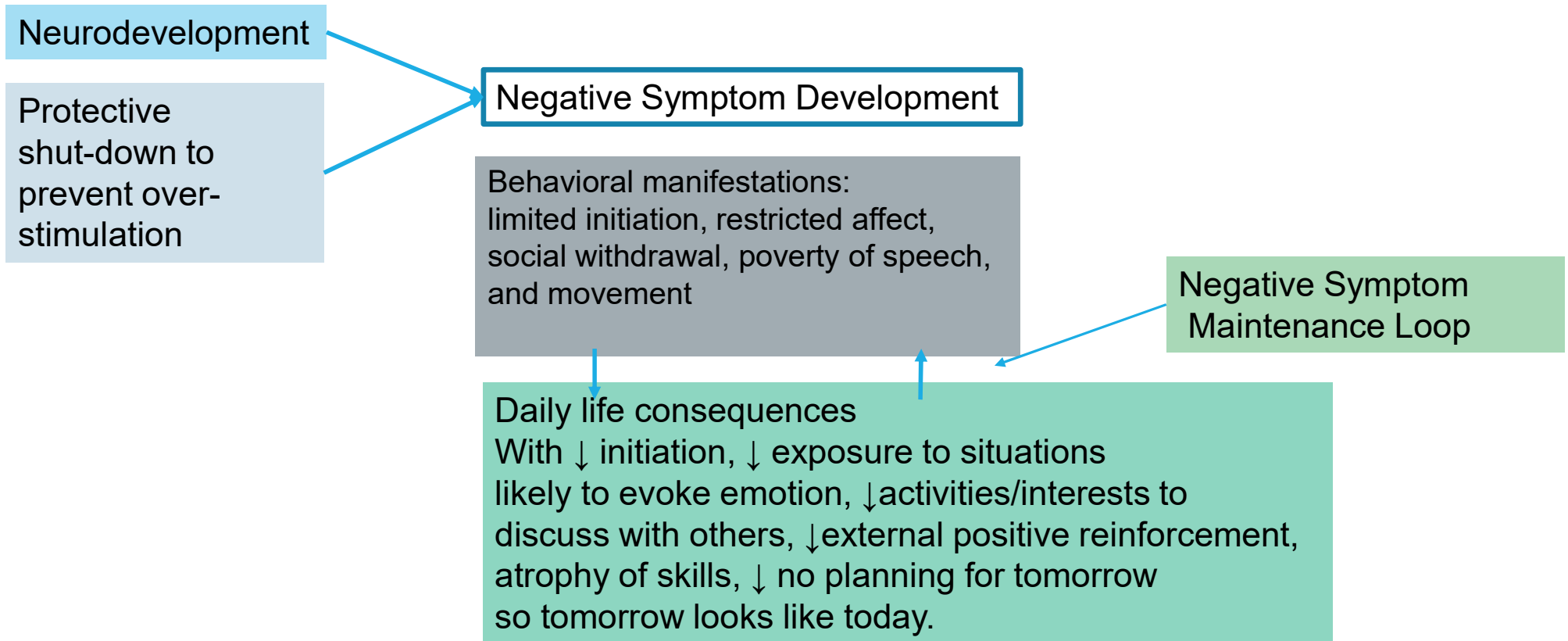Lack of initiation, interest and persistence in social, work and daily activities

Blunted affect
Restriction in range and expression of emotion (facial, vocal, and gestures)

Alogia
Poverty of speech and lack of spontaneous elaboration

Kirkpatrick & Galderis, 2008;World Psychiat 7 (3) 142-147; Buchanan, 2007; Schiz Bul; 33 1013-1022; Blanchard et al. Schizophr Res. 2005 15;77(2-3):151-65.

Model of negative symptom development

Neurodevelopment

Protective shut-down to prevent over-stimulation

Negative Symptom Development

Behavioral manifestations:
limited initiation, restricted affect, social withdrawal, poverty of speech, and movement

Negative Symptom Maintenance Loop

Daily life consequences
With ↓ initiation, ↓ exposure to situations likely to evoke emotion, ↓activities/interests to discuss with others, ↓external positive reinforcement, atrophy of skills, ↓ no planning for tomorrow so tomorrow looks like today.

MOVE:
A Manualized 5-Component treatment Designed to Address All Domains of Persistent Negative Symptoms

1. Antecedent Control based on Cognitive Adaptation

Ann's Daily Checklist
1. Shower
2. Brush Teeth
3. Use Deodorant
4. Take Medication
5. Call Thomas
6. Daily Housekeeping Chore
   (Check Calendar)
7. Play Guitar

Velligan et al. 2015 Schizophr Res 165(0) 175-1800

MOVE:
A Manualized 5-Component treatment Designed to Address All Domains of Persistent Negative Symptoms

2. Anticipatory Pleasure

Velligan et al. 2015 Schizophr Res 165(0) 175-1800

MOVE:
A Manualized 5-Component treatment Designed to Address All Domains of Persistent Negative Symptoms

3. Emotional Processing and Social Cognition

Emotions are directly discussed during and immediately following various work, leisure, and social activities. Practice with identifying emotions and making good guesses about the emotions of others occurs using both computer exercises and in vivo practice in real-world settings. Using programs based on Social Cognition Interaction Training (SKIT) and Mary Eddie Bill.

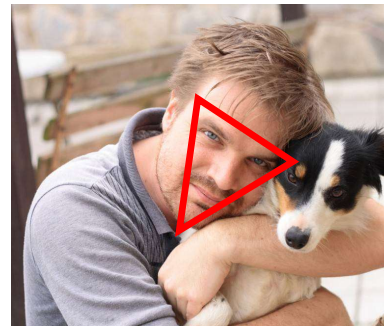|		
Problems in making good guesses about the emotional states of others and to understand the subtleties of conversation make it difficult to initiate and maintain social relationships	When interactions lack matching and reciprocity, it is difficult for individuals feel connected to and interested in the other person.	As with all of MOVE exercises are customized to the persons specific impairments.

Roberts, D. L., & Penn, D. L. (2009).. *Psychiatry research*, *166*(2-3), 141–147. https://doi.org/10.1016/j.psychres.2008.02.007

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Penn et al , 2008 Schiz Bull 2008 May;34(3):408-11. : Velligan et al. 2015 Schizophr Res 165(0) 175-180; Roberts et al 2014 Br J Clin Psychol, 53: 281-298

Mary, Eddy, Bill:
Social Cognition Interaction Training

Simple heuristics to help individuals identify characteristic ways of being.
- My Fault Mary, Blaming Bill, Easy Eddy
- Each with Characteristic thoughts feelings and actions that go with them
- Helps individuals identify their own attributional styles

MOVE:
A Manualized 5-Component treatment Designed to Address All Domains of Persistent Negative Symptoms

4. CBT to address self-defeating thoughts

Negative cognitions that prevent initiation and engagement are actively addressed using CBT techniques as described by Beck et al.

Defeatist beliefs regarding success mediate the relationship between cognitive impairment and both negative symptoms and functioning

Data demonstrate the efficacy of CBT in reducing negative appraisals in individuals with schizophrenia

Rector et al., 2005 Canadian Journal of Psychiatry, 50(5), 247-57;Gumley et al., 2006 British Journal of Clinical Psychology, 45 (Pt 2), 247-60

MOVE:
A Manualized 5-Component treatment Designed to Address All Domains of Persistent Negative Symptoms

4. CBT to address self-defeating thoughts

Granholm---uses an easy heuristic: **Catch It—Check It—Change It**

Unhelpful thought	What is the evidence?	More helpful thought
• They probably don't like me	• I really don't know what they will think • They are smiling so many be they are ok with me	• I can try my new skills and see

Granholm et al., 2014 *J Consult Clin Psychol*. 2014;82(6):1173–1185.

MOVE:
A Manualized 5-Component treatment Designed to Address All Domains of Persistent Negative Symptoms

5. Skill Building

Applies to social skills and independent living skills. Specific areas relevant to the client's day to day experience are utilized (e.g. returning an item to a store, making an appointment to get a hair cut). All techniques used in the persons real environment.

Smile and say Hi

Free things to do....

Bellack et al., 2004 Social skills training for schizophrenia: A step-by-step guide. 2nd Edition. New York: The Guilford Press;Liberman et al; 2002 Psychiatry, 65(2), 137-55.

Pilot Randomized trial of MOVE versus standard community care

Moderate Effect
Labor Intensive
Difficult to Recruit

NSA Mean over time by Treatment

Common X Baseline

3 Months   6 Months   9 Months
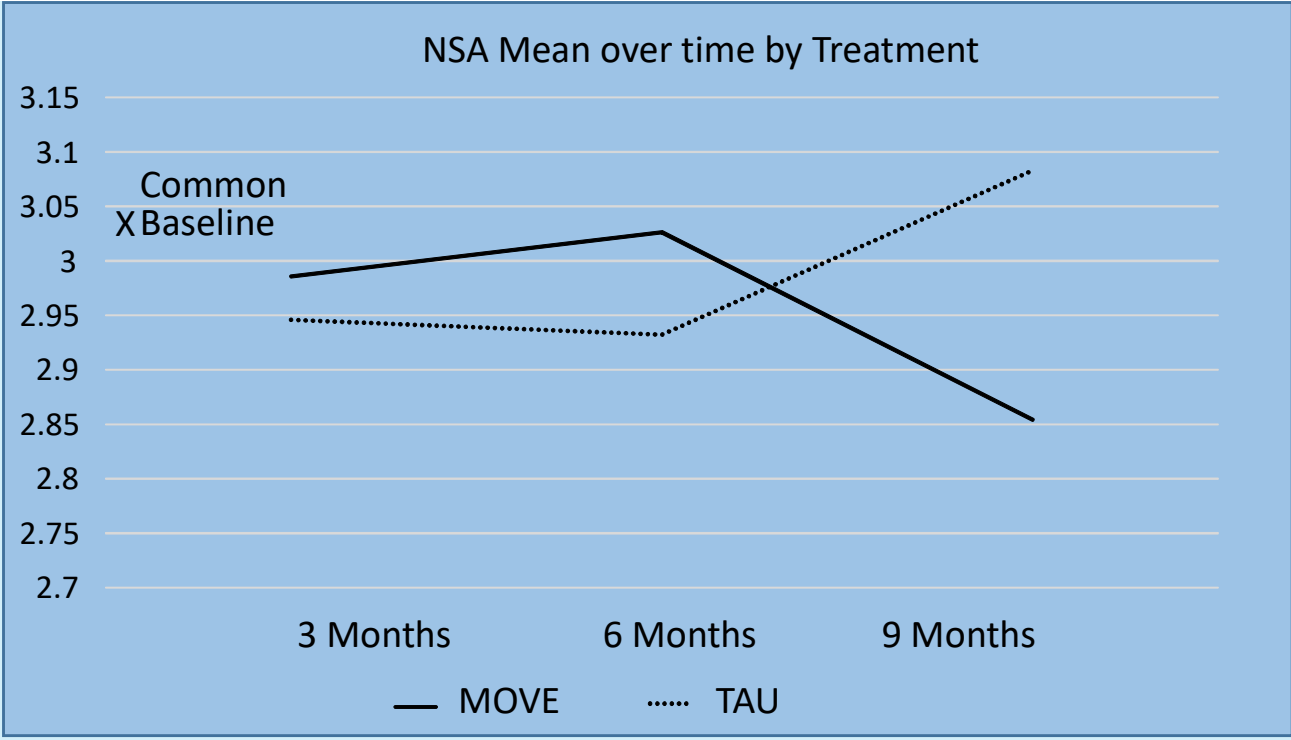
——— MOVE   ······ TAU

- Mixed effects regression model examining NSA mean score over time (3,6,9 months) by treatment group (MOVE / TAU) yielded no significant effects of group ($F_{(1,38)}=.06$ $p<.80$) or time ($F_{(2,76)}=0.03$ $p<.97$); a significant group by time interaction ($F_{(2,76)} =4.09$ $p<.02$).
- Strong trends for group by time only for socialization and motivation subscales ($P<.06$).

Other evidence-based interventions for psychosis

- Peer-to-peer programs
- Clubhouse
- Social Skills Training
- Intensive care management
- Dialectical Behavior Therapy

Hope for the future

- Increasing the uptake of evidence-based interventions. These are not widely adopted by the agencies that see the greatest number of individuals with psychosis

- Increased first episode programs to keep people working and in school; prevent disability

- Ensuring fidelity to the treatment models: training is not enough

- Increased funding for mental health to ensure adoption and skilled use of evidence-based non-medication treatments.