Canadian
Consortium for
Early Intervention
in Psychosis

Functional Recovery in Psychosis in the Context of Early Intervention in Psychosis

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Need For Definition

1. Terms used: Functioning, Functional outcome; Recovery; Functional recovery
2. Functioning is part of the overall concept of recovery but does not replace the concept of recovery. Recovery is more than functioning.
3. Functioning usually encompasses work and-or education, social relations, family relations, friendships, civic participation, social inclusion, ability to live alone etc.

Defining Recovery

1. Lack of consensus on definition of recovery
2. Clinical-academic and utilitarian definitions of recovery
3. Consumer driven recovery definitions, later supported by policy and even service providers: ”Story Line”; “Narratives of Recovery influencing policy (“Recovery Works”)
4. Little effort at an evidence base for narrative definitions
5. Other aspects not well investigated (Social justice, civic participation, safety, economic contribution and not just survival etc)
6. It may disadvantage patients if we exaggerate the rates of recovery through redefining them (e.g. reduction in benefits)

Defining Recovery

1. Clinical: Remission of symptoms (positive, negative, depression, anxiety); Relapse; Physical health; Hospitalization; Mortality (suicide, excess medical disorders)
2. Functional: Work-Education; Housing; Self-care and self-sufficiency; Social and personal relationships; Other role functions (caretaking for elderly parents or partner, homemaking, childcare)
3. Personal (subjective): 'Illness' (meaning, control, stigma), Social (relationships), well-being (physical, psychological, existential, spiritual), economic (job, housing, education); Personal growth

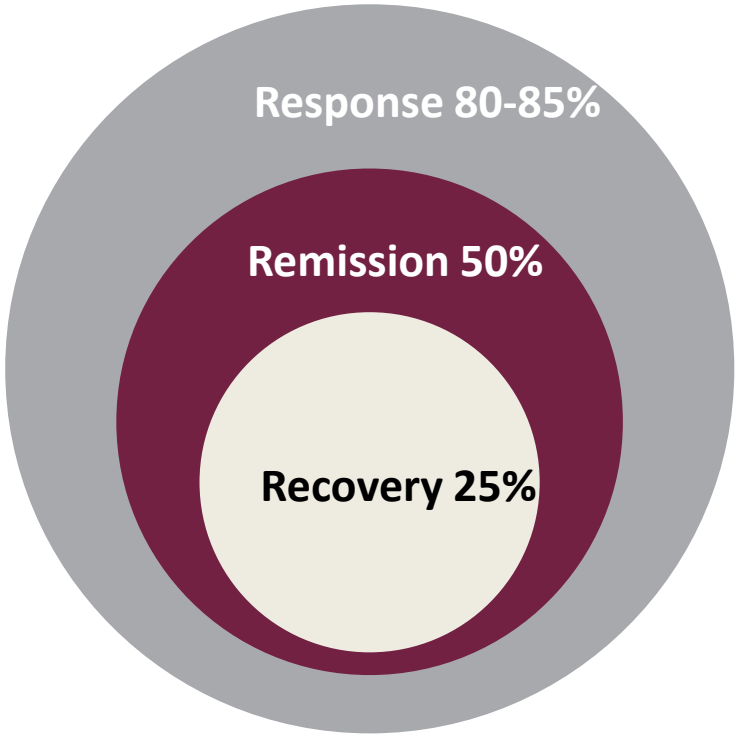
Social Inclusion (World Bank definition)

"The process of improving the terms on which individuals and groups take part in society - improving the ability, opportunity, and dignity of those disadvantaged on the basis of their identity…free from barriers that prevent them from fully participating in political, economic, and social life."

Course, Prognosis And Outcome (Heterogeneity, Multiple Trajectories)

1. At least four different trajectories of clinical outcome (single episode (15-20%), recurring episodes with no significant deterioration (25-30%), recurrent episodes with increasing deterioration (30-50%), no response and treatment resistant (5-15%) (Harrow et al 1997; Robinson et al 2004)
2. Functional (vocational and social) outcome also has multiple long-term trajectories (Velthrost et al 2018; Harrow et al 1997)
3. Most long-term trajectories of outcome are established early in the course of illness (Harrison et al 2001)

Levels of Outcome and Gaps



- **Response:** percentage decrease in or remission of positive symptoms
- **Remission (APA consensus):** SAPS-SANS global rating ≤2 or PANSS item ratings of ≤3 sustained for 6 months
- **Recovery:** independent functioning (work, school, social relationships, independent living), requiring minimal or no support (societal perspective), and personal sense of well-being (personal perspective)

SAPS=Scale for the Assessment of Positive Symptoms; SANS=Scale for the Assessment of Negative Symptoms; PANSS=Positive and Negative Syndrome Scale

Andreasen et al. (2005) *Am J Psychiatry*;162(3):441–449

Remission and Recovery: What do we know now

1. 75 studies, 19072 patients, mean follow-up 5.5 ys. For remission and 7.5 ys for recovery
2. Pooled rate of remission (APA definition): 58% (56% Schizophrenia spectrum; 78% Affective Psychosis)
3. Recovery (Functional-social, occupational, educational most with symptom remission): 38% (CI 30-46%)

(Syst. Meta-anal Review (Lally et al, 2017, BJP)

Remission and Recovery: Key Messages

1. **Increase in rates of remission over time** (probably coinciding with EIS development)
2. Higher rates in Canada-USA; Asia and Africa vs Europe (Mixed reasons)
3. **No increase in recovery rates over time**
4. Remission rates and recovery are sustained over time after the first two years. Trajectories are established early
5. Gap between remission and recovery rates are a source of concern

(Syst. Meta-anal review Lally et al, 2017, BJP)

Trajectories of Long-term Outcome

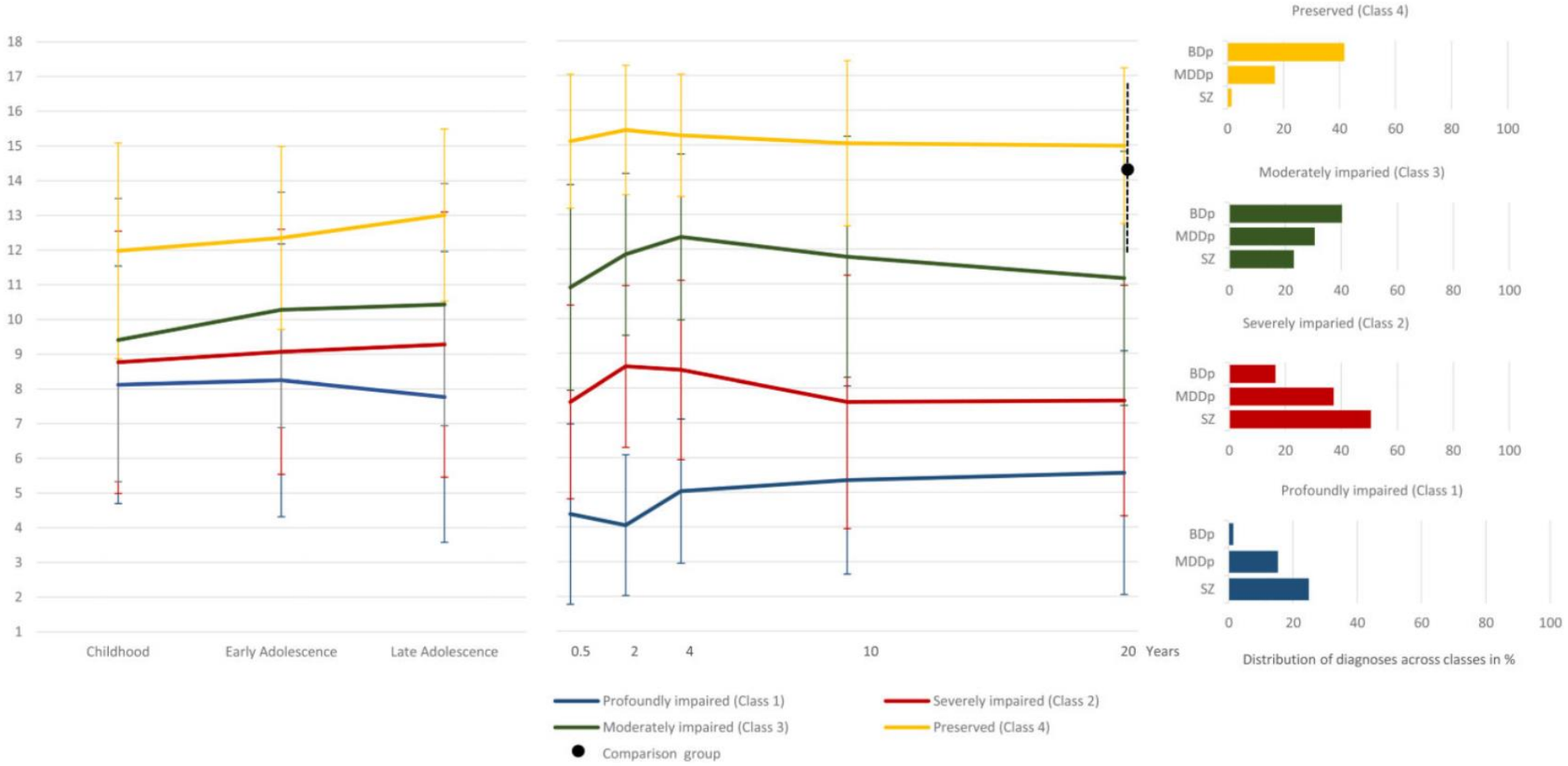


Figure 2. Trajectories of functioning across psychotic disorders derived from Latent Class Growth Analyses
Abbreviations: SZ=schizophrenia spectrum disorder; BDp =bipolar disorder with psychosis; MMDp = major depression with psychosis

Velthorst et.al. Am J Psychiatry. 2017 Nov 1;174(11):1075-1085

Change in clinical and functional outcome over the first five years; 2 years vs 5 years: RCT (Malla et al 2017; Mustafa et al 2021)

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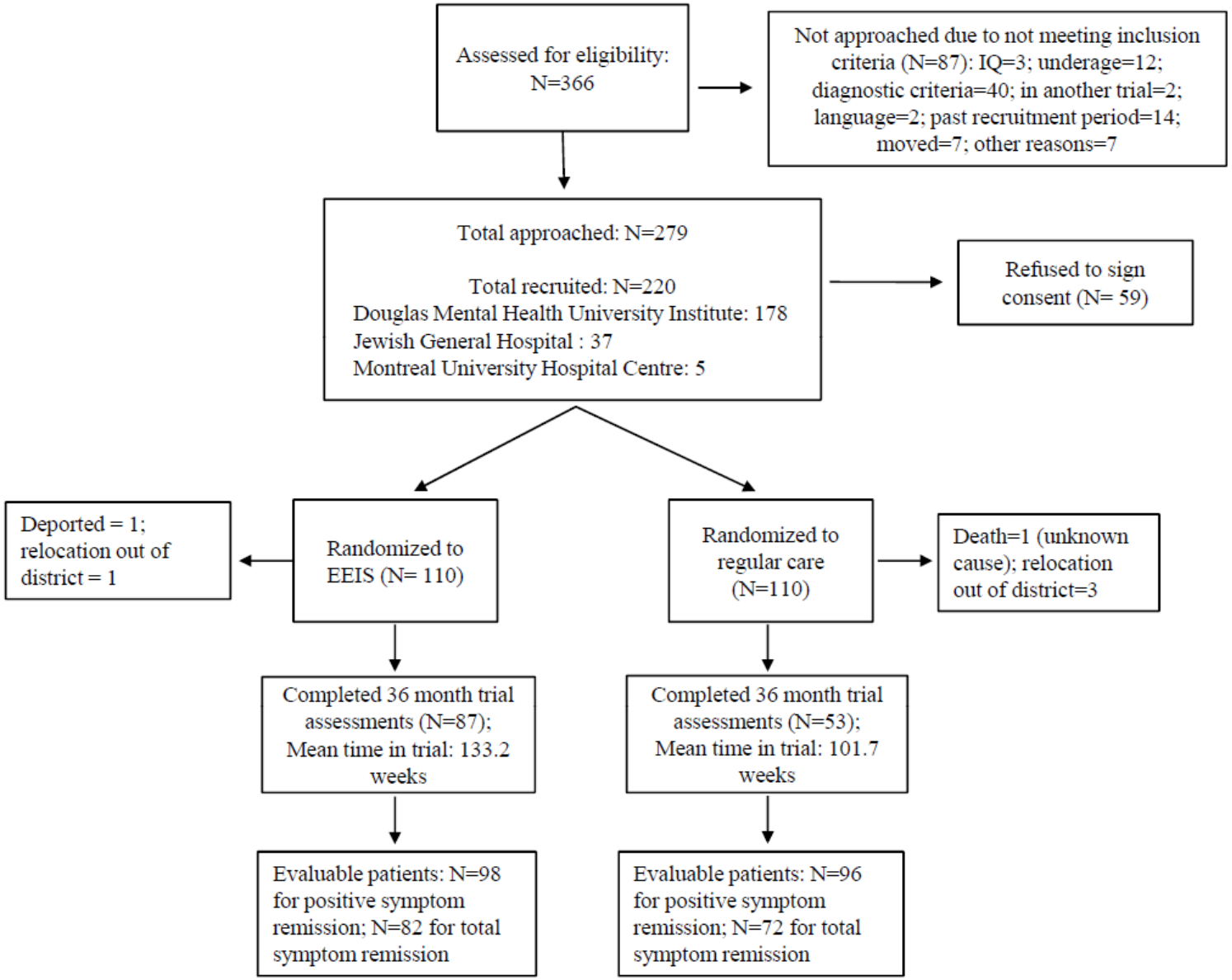
ORIGINAL ARTICLE

Unfinished business: Functional outcomes in a randomized controlled trial of a three-year extension of early intervention versus regular care following two years of early intervention for psychosis

Sally S. Mustafa[1] | Ashok Malla[1,2] | Ridha Joober[1,2] | Sherezad Abadi[3] | Eric Latimer[2,3] | Norbert Schmitz[2,3,4] | G. Eric Jarvis[2,5] | Howard C. Margolese[2,6] | Nicola Casacalenda[2,5] | Amal Abdel-Baki[7] | Srividya N. Iyer[1,2]


Assessed for eligibility: N=366
Not approached due to not meeting inclusion criteria (N=87): IQ=3; underage=12; diagnostic criteria=40; in another trial=2; language=2; past recruitment period=14; moved=7; other reasons=7
Total approached: N=279
Total recruited: N=220
Douglas Mental Health University Institute: 178
Jewish General Hospital : 37
Montreal University Hospital Centre: 5
Refused to sign consent (N= 59)
Deported = 1; relocation out of district = 1
Randomized to EEIS (N= 110)
Randomized to regular care (N=110)
Death=1 (unknown cause); relocation out of district=3
Completed 36 month trial assessments (N=87); Mean time in trial: 133.2 weeks
Completed 36 month trial assessments (N=53); Mean time in trial: 101.7 weeks
Evaluable patients: N=98 for positive symptom remission; N=82 for total symptom remission
Evaluable patients: N=96 for positive symptom remission; N=72 for total symptom remission

Functional Recovery: Two years outcome vs 5 years outcome (Results of PEPP RCT)

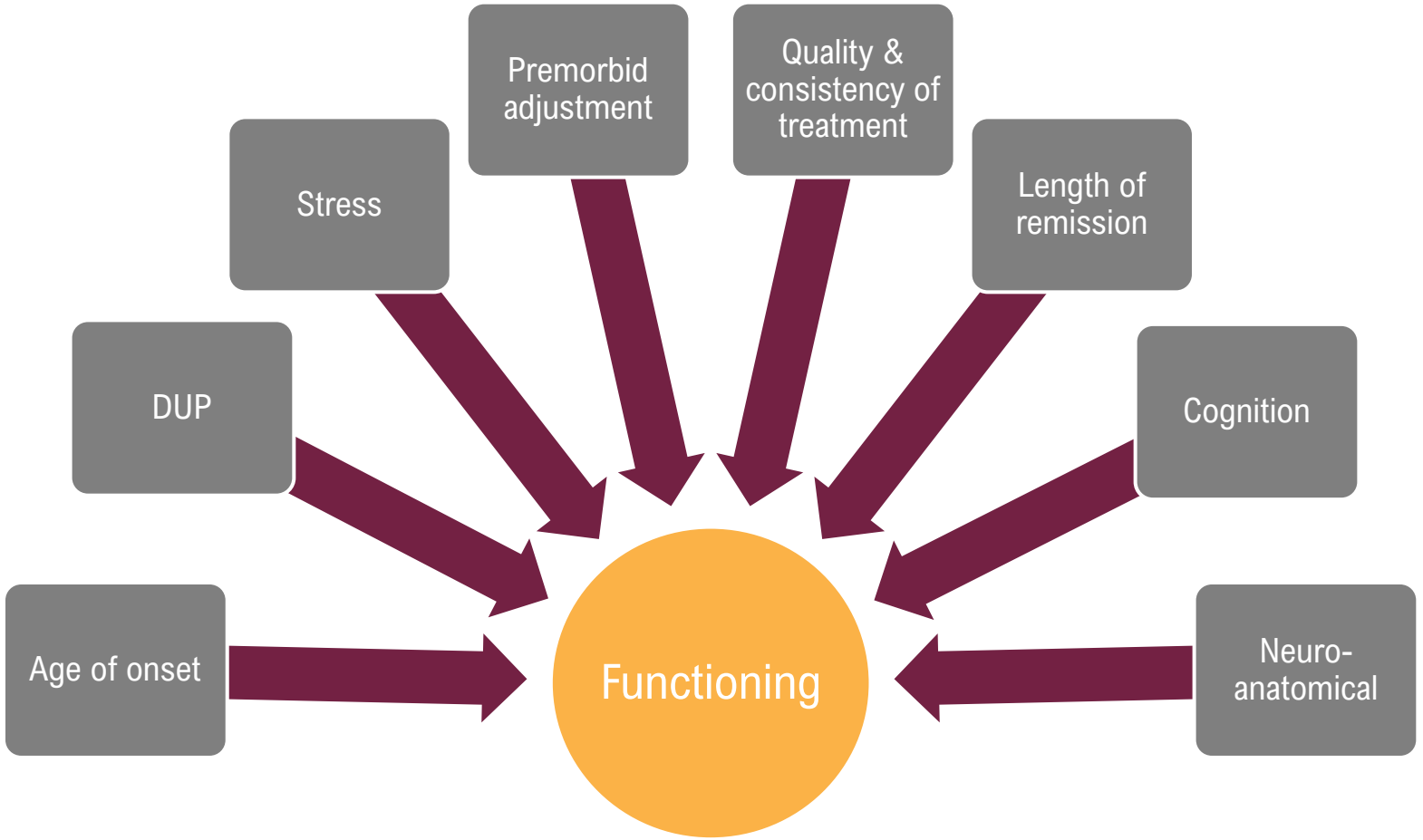
1. Over the study period of 3 years length of remission of symptoms was greater in extended EIS group vs regular care between year 2 and year 5
2. **No parallel increase** in time spent in functional recovery (SOFAS >60) in either *Extended EI* (Mean 50.1 vs 46.18 weeks) or in *Regular care*
3. **No increase** in rates of employment-enrollment in education in either *Extended EI* or in *Regular care* (60.4% vs 68.8%) from year 2 to year 5.
4. Remission of symptoms and years of education remain the best predictors of either of these outcomes irrespective of treatment condition (EEI or RC)

(No difference at the time of randomization).

(Mustafa et al Acta Psychiatrica Scand 2021 in press; Malla et al 2017)

PREDICTORS AND MARKERS OF COURSE AND OUTCOME ON RECOVERY
(Guide for focused interventions early)

What predicts functional outcome? Which of these are malleable and which are not?



Predictors of Functional Outcome: A systematic and Meta-analytical Review

1. 50 Eligible Studies; 6669 patients
2. ***Significant predictors independent of other known influences***: **DUP (Delay in treatment of psychosis); Remission of Positive and Negative Symptoms; Cognition** (Overall cognition, Verbal fluency) and **specifically verbal memory (**Attention; Processing Speed)
3. ***Not independently associated with functional outcome***: age at onset or at first treatment; diagnosis SSD or APs, insight, medication adherence, neuroimaging markers, substance abuse
4. Being **Female and Level of education** is associated with overall functioning but **not to** vocational outcome
5. Length of prior work experience (? Modified by age)

Santesteban-Echarra et al 2021, Clinical Psychol. Rev.- in press

A Proposed Model to Sort Out the Puzzle

Capacity Variables

- Sex (Male or Female)
- Premorbid functioning (social and academic)
- Age at onset of first episode of psychosis
- Cognition (Verbal memory) prior to treatment

Pre-Treatment Variables

- Duration of untreated psychosis (DUP) (Delay in treatment)

Overall Functioning (work, social)

Treatment Variables

- Antipsychotic medication adherence
- Quality of Treatment?

Treatment Outcomes

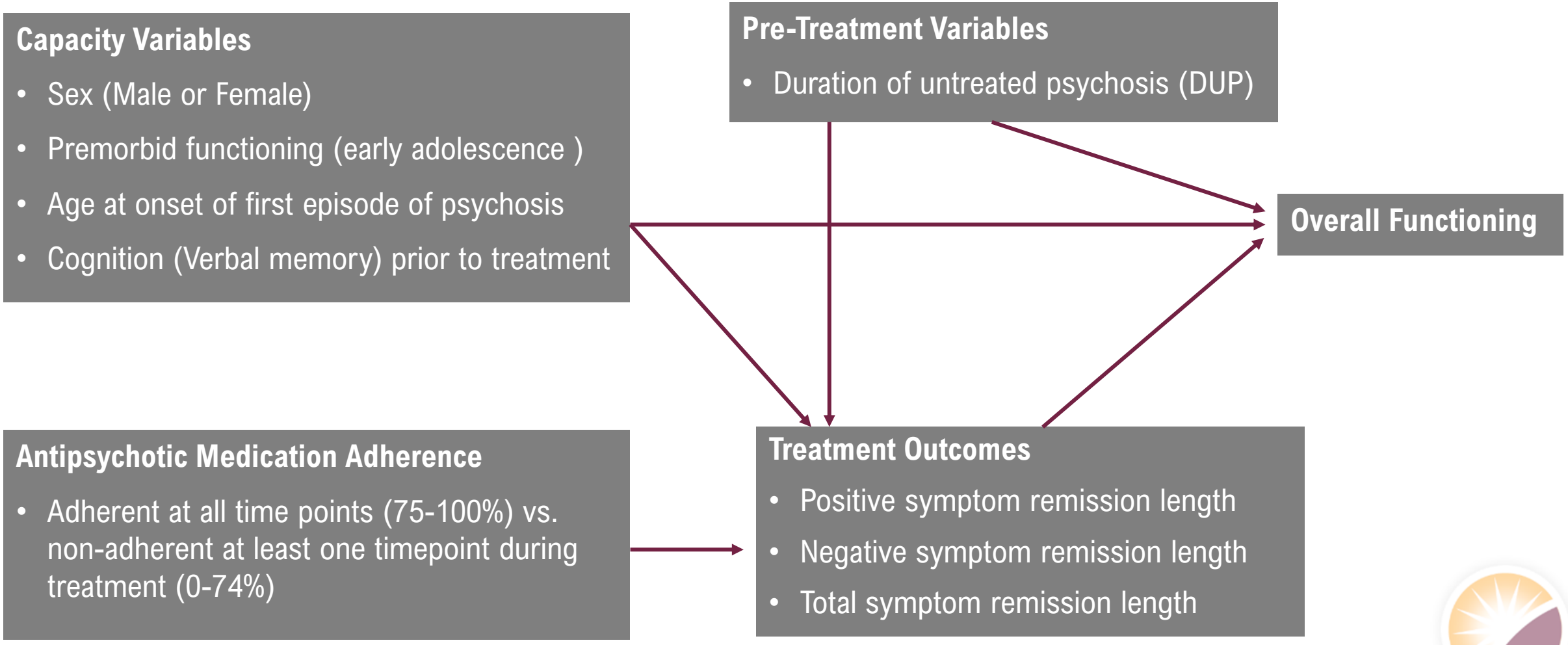
- Positive symptom remission length
- Negative symptom remission length
- Total symptom remission length

Questions

- How do **capacity variables** (cognition, grey matter, Premorbid adjustment) influence outcome?
- Do capacity variables interact with each other or with other **pre-treatment** and **treatment variables** to influence outcome?
- Is outcome influenced by **nature, quality and consistency** of treatment? How do capacity and other pre-treatment variables interact with treatment to influence outcome?

Schematic Presentation Of How Predictors May Work In A Complex Set Of Relationships

A Proposed Model to Sort Out the Puzzle



Posttraumatic Growth Following A First Episode Of Psychosis: Domains

1. Improved health, stronger sense of self and improved personality
2. Stronger, more balanced spirituality and religiosity
3. Improved relationships with others
4. Improved lifestyles, new goals and expectations for the future

"*It's (psychosis) brought me a lot closer to who I am, and it has changed my personality in the way that I feel. I'm a much more open and receptive person whereas before I was someone who was really just shut down and self-centered.*"

Jordan G., Iyer SN., Malla A. (2019). "It's brought me a lot closer to who I am": aspects of positive change following a first episode of psychosis. *Frontiers in Psychiatry. doi:* https://www.frontiersin.org/articles/10.3389/fpsyt.2019.00480/full

Summary

- Functional outcomes are part of the larger concept of recovery (others being clinical and personal)
- Rates of remission (clinical recovery) **have** increased recently, likely associated with EIS
- Rates of Functional Recovery remain low (30-40%) and have **not** increased unlike remission rates
- Long-term trajectories of clinical and functional outcome are established within the first two years although clinical outcome continues to show further improvement, especially negative symptoms.

Summary

- Predictor are multiple and most of the variance in outcome is associated with unexplored variables (environmental contexts, quality of treatment and natural variation)
- Some **malleable** predictors of functional outcome can be specifically targeted to improve recovery rates (e.g. Reducing DUP, Sustaining symptom remission, Improving cognition through cognitive retraining)
- Reducing the gap between remission and recovery will require specific interventions to increase skills and opportunities (e.g. employment support programs, housing stability, treatment of comorbid conditions, family intervention) to begin **very early** preferably within the first year of treatment
- Recovery must include multiple dimensions including personal and subjective well being as well as social justice, civic participation, personal growth, social inclusion etc.

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Questions?

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