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From Unmet Need to Reality

Roluperidone is potentially the first treatment for negative symptoms of schizophrenia

KOL Event | November 12, 2026

Forward-Looking Statement

This presentation contains forward-looking statements which are subject to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995, as amended. Forward-looking statements are statements that are not historical facts, reflect management's expectations as of the date of this presentation, and involve certain risks and uncertainties. These statements may be identified by words such as "aims," "anticipates," "believes," "could," "estimates," "expects," "forecasts," "goal," "intends," "may," "plans," "possible," "potential," "seeks," "will" and variations of these words or similar expressions that are intended to identify forward-looking statements, although not all forward-looking statements contain these words. Forward-looking statements in this presentation include, but are not limited to, statements with respect to the clinical development of roluperidone; the potential therapeutic benefits and market opportunities of roluperidone; Minerva's expectations regarding the confirmatory clinical trial of roluperidone and related regulatory developments; Minerva's belief that it has reached alignment with the U.S. Food and Drug Administration ("FDA") on the Phase 3 confirmatory trial of roluperidone for the treatment of negative symptoms of schizophrenia; the timeline and results of the Phase 3 confirmatory trial; regulatory review and approval of roluperidone to be marketed in the United States and elsewhere; and management's ability to successfully achieve its goals. These forward-looking statements are based on our current expectations and may differ materially from actual results due to a variety of factors including, without limitation, trials and studies may be delayed and may not have satisfactory outcomes, and earlier trials and studies may not be predictive of later trials and studies; the design and rate of enrollment for clinical trials, including the current design of the Phase 3 confirmatory trial evaluating roluperidone may not enable successful completion of the trial(s); the commercial opportunity for roluperidone in negative symptoms of schizophrenia may be smaller than anticipated; Minerva may be unable to obtain and maintain regulatory approvals; Minerva may experience uncertainties inherent in the initiation and completion of clinical trials and clinical development; the need to align with collaborators or partners may hamper or delay development and regulatory efforts or increase costs; uncertainties of patent protection and litigation; and general economic conditions. Other factors that may cause our actual results to differ from those expressed or implied in the forward-looking statements in this presentation are identified under the caption "Risk Factors" in our filings with the Securities and Exchange Commission (the "SEC"), including our Annual Report on Form 10-K for the year ended December 31, 2025, filed with the SEC on March 11, 2026, as may be updated by subsequent 10-Qs. Copies of reports filed with the SEC are posted on our website at www.minervaneurosciences.com. The forward-looking statements in this presentation are based on information available to us as of the date hereof, and we expressly disclaim any obligation to update any forward-looking statements, except as required by law.

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Welcome to Today's Presentation: Introductions

Gregory Strauss, PhD
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Remy Luthringer, PhD
Executive Chairman & Chief Executive Officer
Minerva Neurosciences, Inc.

Agenda

- Introduction | Roluperidone clinical data | C19 Study update
  Remy Luthringer, PhD
- Improving primary negative symptoms - the holy grail of schizophrenia treatment
  Gregory Strauss, PhD
- Primary negative symptoms in the clinic
  Brian Kirkpatrick, MD, MSPH
- New analyses strengthening uniqueness of roluperidone in treating negative symptoms
  Remy Luthringer, PhD
- Transdiagnostic nature of negative symptoms supporting the promise of addressing unmet needs beyond schizophrenia
  Christoph Correll, MD
- Market Opportunity | Concluding Remarks
  Remy Luthringer, PhD
- Q&A

Introduction | Roluperidone clinical data | C19 Study update



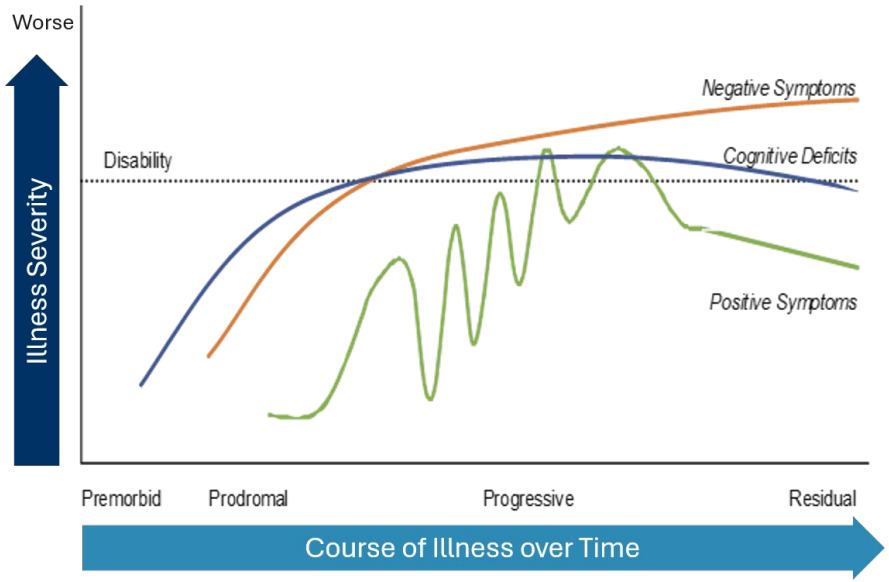
Remy Luthringer, PhD

Executive Chairman & Chief Executive Officer
Minerva Neurosciences, Inc.

The Central Role of Negative Symptoms of Schizophrenia

Primary Negative Symptoms

- Primary negative symptoms include deficits of:
  - Ability to express emotion (blunted **Affect**)
  - Conversation ("poverty of speech", **Alogia**)
  - Purposeful activities (**Avolition**)
  - Capacity for social interactions (**Asociality**)
  - Ability to experience pleasure (**Anhedonia**)
- Primary negative symptoms are associated with the underlying pathophysiology of schizophrenia.



Source: Correll and Schooler, 2020[1]

Secondary Negative Symptoms

- Patients treated with dopamine blocking antipsychotics often experience adverse effects which are drug- induced secondary negative symptoms, in addition to continuing to experience primary negative symptoms. Secondary symptoms are a leading reason why most patients dislike and eventually discontinue treatment with antipsychotics.[2]
- Even for patients with stable positive symptoms, most continue to have moderate to severe negative symptoms that significantly impair their daily functioning whether they are being treated with antipsychotics or not.

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[1] Correll CU, Schooler NR. Negative Symptoms in Schizophrenia: A Review and Clinical Guide for Recognition, Assessment, and Treatment. *Neuropsychiatr Dis Treat.* (2020); [2] Lieberman JA, et al. Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. *NEJM* (2005)

Negative symptoms, not positive symptoms, are the primary drivers of disability in schizophrenia

> *"While positive symptoms are often the most recognized features of schizophrenia due to their external observation of distorted normal function,* ***negative symptoms*** *are the lack of normal functions that* ***differentially affect schizophrenia treatment and prognosis.***" [1]

Negative Symptoms

- Associated with lower functioning
- Associated with lower Health-Related Quality of Life (HRQoL)

Improved functioning associated with improved HRQoL[1]

80%–90% of people with schizophrenia are **unemployed**[2,3,4,5]

vs. ~4–5% in the general population

Negative symptoms; not positive symptoms drive disability in schizophrenia[6]

Consistent finding across >25 studies; yet no approved treatment targets negative symptoms

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[1] Chan A et al., Assoc between negative symptoms and HRQoL and functional outcomes in persons with schizophrenia. *Schizophrenia Research* (2026); [2] Evensen S et al. Prevalence, Employment Rate, and Cost of Schizophrenia in a High-Income Welfare Society. *Schizophr Bull.* 2016;42(2):476–483; [3] Holm M et al. Employment among people with schizophrenia or bipolar disorder. *Acta Psychiatr Scand.* (2021); [4] Rosenheck R et al. Barriers to Employment for People With Schizophrenia. *Am J Psychiatry.* (2006); [5] Davidson M et al. Nation-Wide Study on Percentage of Schizophrenia and Bipolar Disorder Patients Who Earn Minimum Wage or Above. *Schizophr Bull.* (2015); [6] Rabinowitz, J et al. Negative symptoms have greater impact on functioning than positive symptoms in schizophrenia: Analysis of CATIE data. *Schizophrenia Research* (2012).

Roluperidone: designed to avoid the detrimental side effects of antipsychotics while treating negative symptoms and keeping positive symptoms stable

- Nearly all current antipsychotics block dopamine, resulting in[1]:
  - interference with the brain reward circuits or amotivation,
  - sedation,
  - motor side effects, and
  - prolactin elevation.

In contrast, roluperidone lacks antagonistic activity at the dopamine receptor.

- Roluperidone is a cyclic amido derivative with antagonistic affinities for[1,2]:
  - Serotonin 5-HT_{2A},
  - $Sigma_2$, and
  - $Alpha_{1A}$-adrenergic.

These multiple affinities may explain roluperidone's ability to improve primary negative while controlling positive symptoms

  - In addition, animal pharmacology suggests that roluperidone may increase the release of brain-derived neurotrophic factor (BDNF) and glial cell line-derived neurotrophic Factor (GDNF)[1,3], both nerve growth factors implicated in neuron survival and growth, which may provide an additional disease modifying effect.

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[1] Luthringer R, Davidson, M, Development of non-dopamine active drugs for negative symptoms. Schizophrenia Research (2026); [2] Davidson M, et al. Roluperidone monotherapy, a treatment for negative symptoms in schizophrenia. *International J Neuropsychopharmacology* (2025); [3] Roluperidone increases in-vitro Brain-Derived Neurotrophic Factor (BDNF) release: a possible mechanistic role in negative symptoms? Poster T145, presented at Schizophrenia Intern'l Research Society (SIRS) Congress in Orlando, FL, on April 11, 2019

C03 & C07 Studies: similar designs and similar results – guiding C19 confirmatory trial

	C03 Study 244 patients	C07 Study 515 patients
Negative symptoms (NSFS)*	**p ≤ 0.001** Statistically significant (64 mg)	**p ≤ 0.043** Nominally significant (64 mg)**†
Function (PSP total score)	**p ≤ 0.002** Statistically significant (64 mg)	**p ≤ 0.016** Statistically significant (64 mg)†

Avoids side effects of antipsychotics, like

- ❑ Metabolic syndrome
- ❑ Sedation
- ❑ Motor symptoms (extra pyramidal symptoms (EPS))
- ❑ Prolactin elevation
- ❑ Nausea

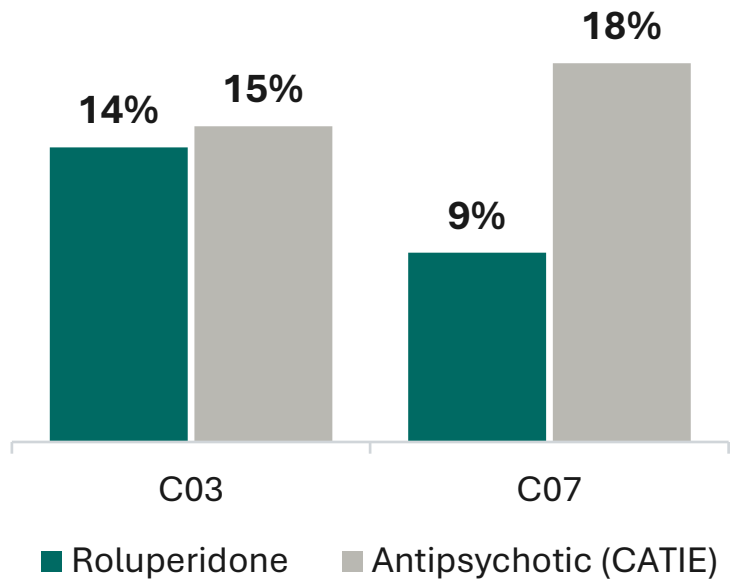
C03 & C017 Studies; 12-week DB efficacy, then OL extension (24 weeks in C03, 40 weeks in C07).

Relapse rate, psychotic symptoms

C03: after 12-week DB + 24-week OL

C07: after 12-week DB + 40-week OL

Roluperidone Studies vs. CATIE[1,2 ††]

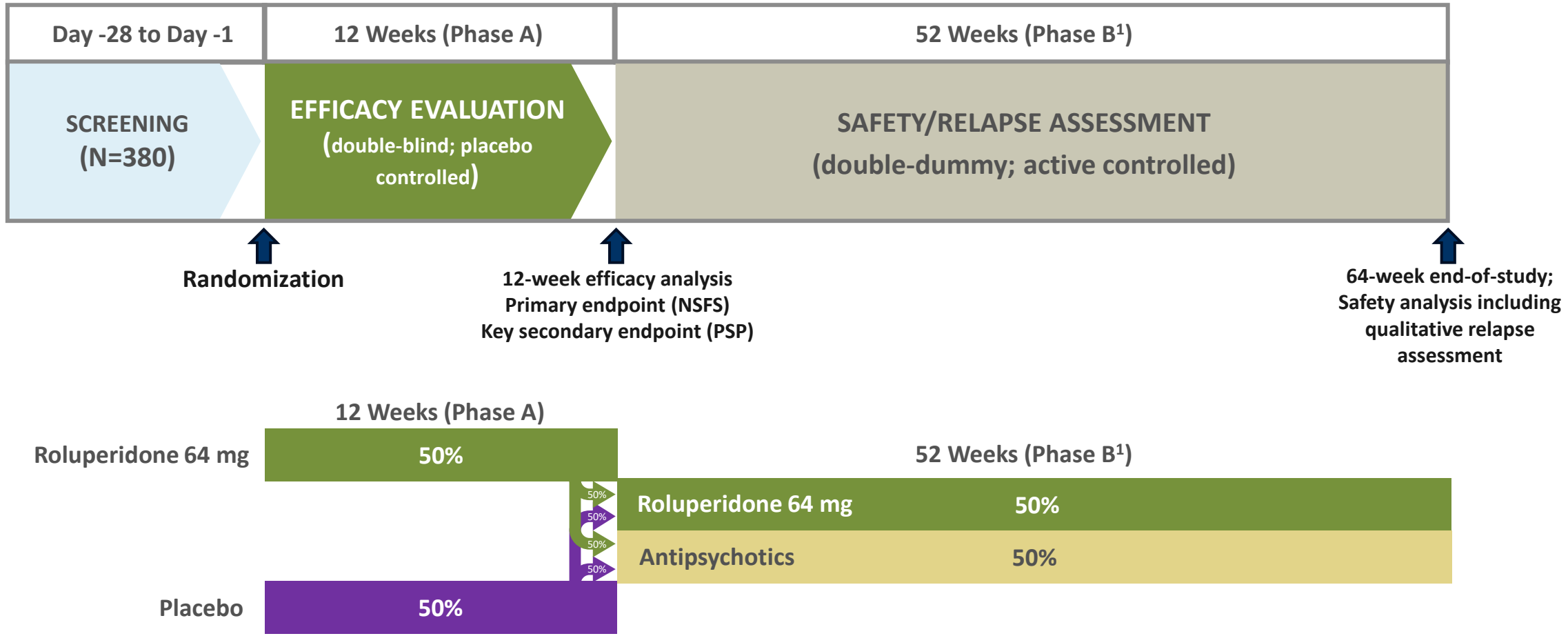


*NSFS was not the primary endpoint of C03 Study but is shown because it is the primary endpoint agreed with FDA for the ongoing C19 Study (the primary endpoint of C03 Study was PANSS Pentagonal-NFS, which also showed a statistically significant improvement (0.004 for 64 mg); **C07 Study's primary endpoint met only on nominal basis (p ≤ 0.043) due to statistical plan's use of Hochberg Type I error correction; †mITT population (excludes 1 site for reasons of implausible data). ††Historical comparison data from CATIE study in patients meeting inclusion-exclusion criteria of Minerva's C03 and C07 studies. [1] Lieberman JA, et al. Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. *NEJM* (2005); [2] Speyer H, et al. Moderate to severe negative symptoms predict low risk of symptoms worsening in schizophrenia patients in CATIE. *Schizophr Res.* (2026). Other source: Minerva Neurosciences.

DB: double-blind. **OL:** open-label extension. **NSFS:** PANSS Marder Negative Symptoms Factor Score. **PSP:** Personal and Social Performance scale.

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C19 Study: ***actively enrolling***



[1] Patients re-randomized to either one of three atypical antipsychotics or roluperidone.

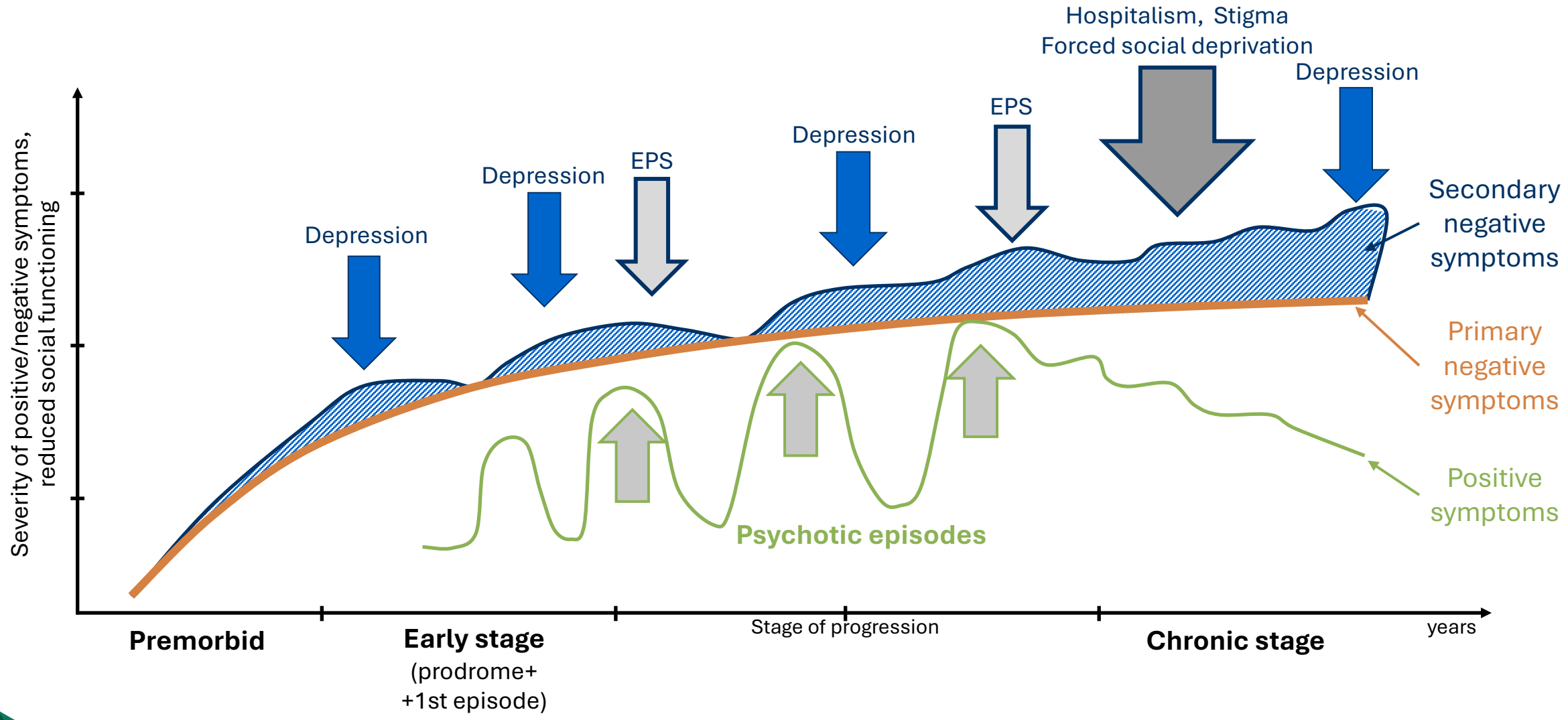
C19 Study: designed to demonstrate an effect on primary negative symptoms & avoid the pseudo–effect seen in studies aiming to treat an acute relapse of positive symptoms

- Challenge of adjunctive treatment studies: Dozens of well-powered academic and industry sponsored trials studying new drugs as add-on to antipsychotics have failed to show an effect on negative symptoms
  - To be effective for negative symptoms, drug would need to improve **primary** *(intrinsic, disease-specific)* without causing **secondary** *(extrinsic)* negative symptoms
  - Study designs that fail to control for secondary negative symptoms might mask an effect on primary-negative symptoms and make it challenging to demonstrate a drug effect on primary negative symptoms
  - Add-on therapy designs ignore the heterogeneity of schizophrenia patients

- Monotherapy studies targeting an appropriate patient population
  - Focus on identifying a treatment effect on primary negative symptoms
  - Avoids confounding improvements driven by secondary negative symptoms
  - Does not interfere with the ability to treat acute episodes of psychosis with antipsychotics if necessary

➢ ***Monotherapy designs are recommended by leading investigators and thought leaders for studies targeting PRIMARY Negative Symptoms to avoid the confounding effects of secondary negative symptoms caused by antipsychotics drugs*** *(ISCTM Negative Symptom Working Group; Marder 2020)*

Studies in acutely relapsed patients are only able to assess a pseudo-improvement of negative symptoms and can't claim that the drug is improving primary negative symptoms



Adapted from: Mosolov S. & Polina Y. Primary and Secondary Negative Symptoms in Schizophrenia. Frontiers in Psychiatry. (2022)

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Improving primary negative symptoms - the holy grail of schizophrenia treatment



Gregory Strauss, PhD

Franklin Professor of Psychology
Department of Psychology, University of Georgia

Negative Symptoms are Heterogeneous

Primary/Disease Related

Negative symptoms as a direct manifestation of schizophrenia

20

SAME SCORE
(e.g., PANSS)

Secondary

Negative symptoms driven by other factors

The same negative symptom score on a rating scale can be observed for very different reasons

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Secondary negative symptoms are driven by factors other than the illness itself

Common causes of secondary symptoms

Mood and anxiety

- **Depression**
- **Anxiety**

Positive symptoms

- **Hallucinations**
- **Delusions**
- **Disorganization**

Medication effects

- **Medication induced sedation**
- **Extrapyramidal symptoms**
  (e.g., parkinsonism, dystonia)



→Treating secondary sources does not improve primary negative symptoms

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Treatment of primary negative symptoms is the holy grail

1 **Primary and secondary phenotypes have distinct underlying mechanisms**

Primary	Secondary
Intrinsic neural mechanisms	Driven by other factors (e.g., mood, anxiety)

2 **Treatments targeting secondary sources often reduce negative symptoms in patients with secondary phenotypes**

e.g., SSRIs, anxiolytics, antipsychotics, anticholinergics

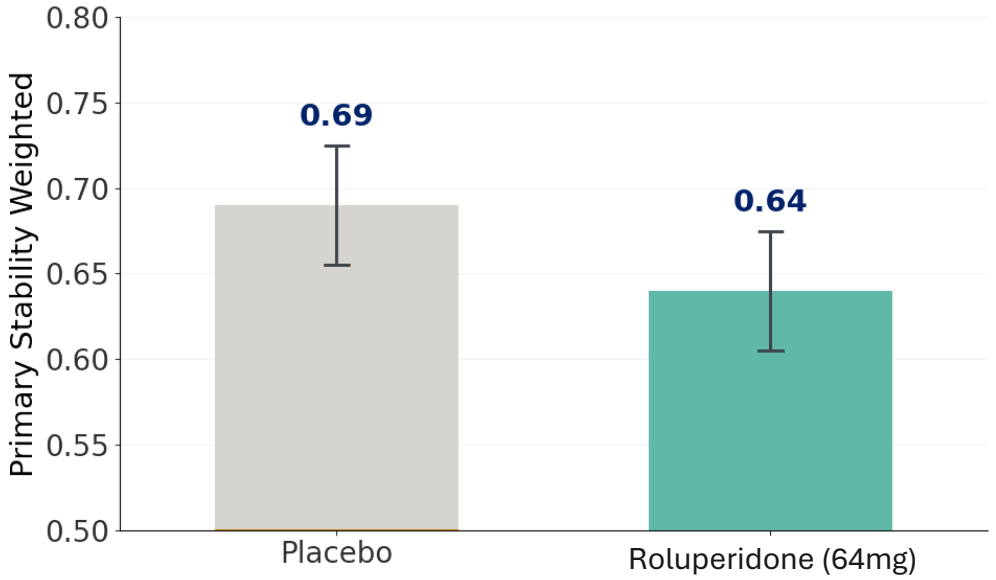
3 **Treatments targeting secondary sources do not reduce negative symptoms in patients with primary phenotypes**

4 **Treatments targeting primary negative symptoms are not expected to reduce negative symptoms in patients with secondary phenotypes**

The C03 and C07 Studies demonstrate roluperidone improves primary negative symptoms

Primary Negative Symptoms

(combined C03 & C07 Studies)

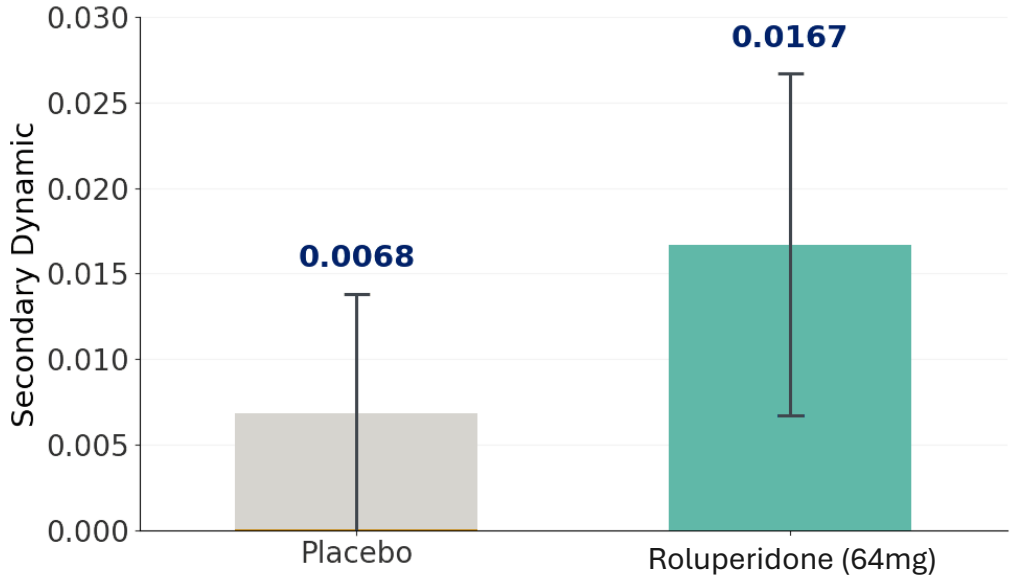


Significant difference vs placebo (p = .031)

Scores reflect persistence of primary negative symptoms from baseline to end of study. Lower scores in roluperidone than placebo reflect greater improvement in primary negative symptoms from drug.

Secondary Negative Symptoms

(combined C03 & C07 Studies)



No significant difference (p = .61)

Scores reflect persistence of secondary negative symptoms from baseline to end of study. Lack of differences indicates Roluperidone and placebo do not differ in how much they reduce secondary negative symptoms.

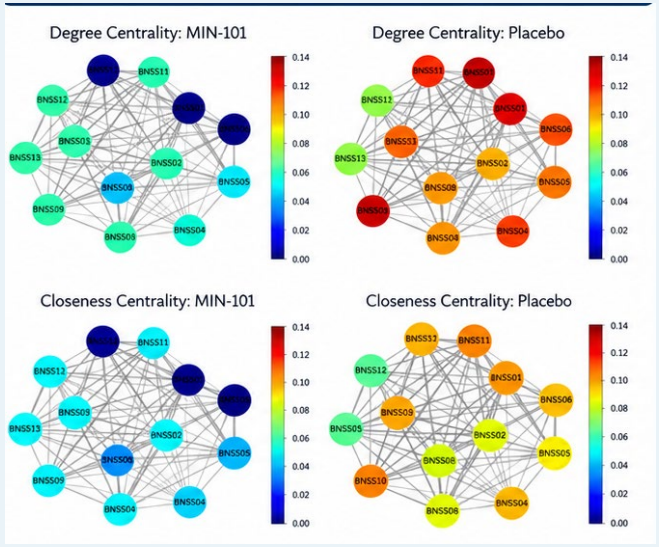
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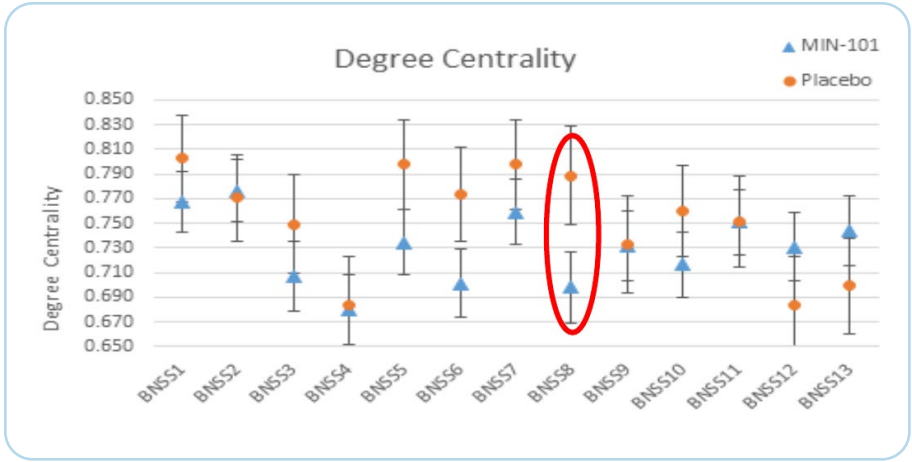
Source: Strauss, GP and Minerva Neurosciences; data on file

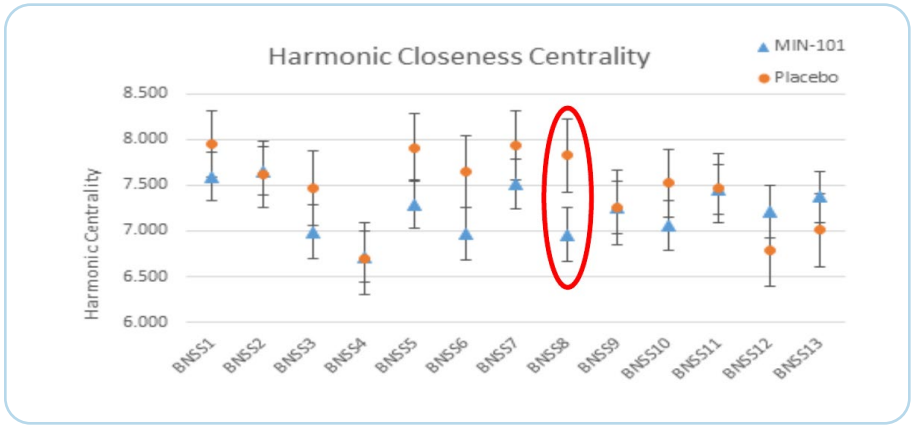
Avolition – the key domain driver for improving negative symptoms

Analysis of C03 Study[1]

Symptom Network Centrality







Key Finding

Centrality Measures:

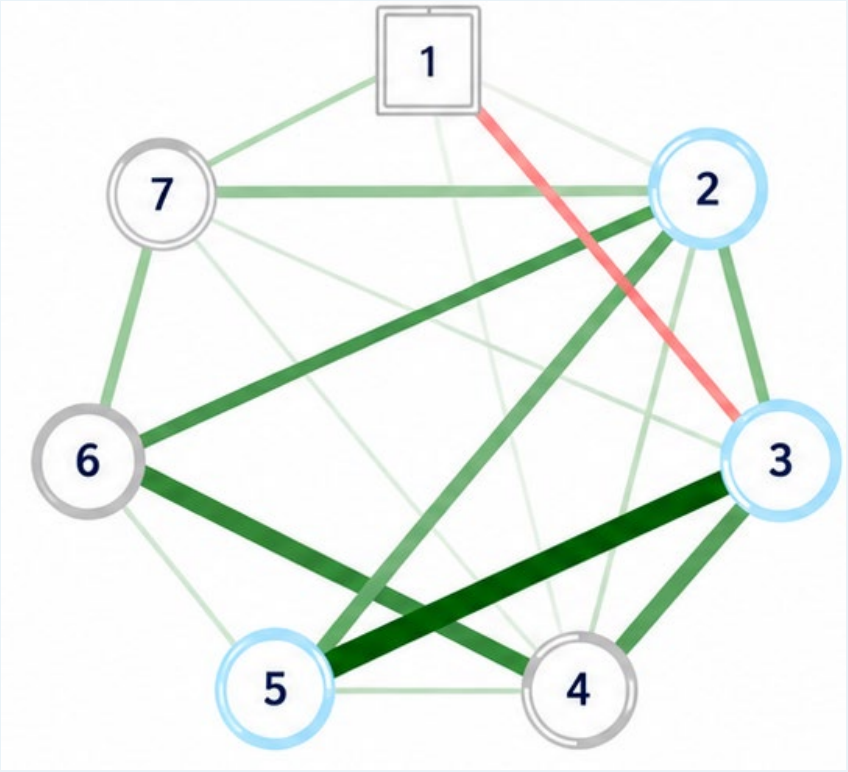
Avolition is the key symptom that leads to improvement

[1] Strauss GP, et al. Network Analysis Indicates that Avolition is Most Central Domain for Successful Treatment of Negative Symptoms: Evidence from Roluperidone Randomized Clinical Trial. *Schizophr Bull.* (2020)

Avolition – the key domain for treatment (REPLICATED)

Analysis of C07 Study[1]

Week 12 Symptom Network



1: Treatment
2: Blunted Affect
3: **Emotional Withdrawal**
4: Poor Rapport
5: Passive Withdrawal
6: No Spontaneity
7: Motor Retardation

Key Finding

Emotional Withdrawal is the key symptom that leads to improvement

WHICH IS THE PANSS ITEM MOST SIMILAR TO BNSS AVOLITION

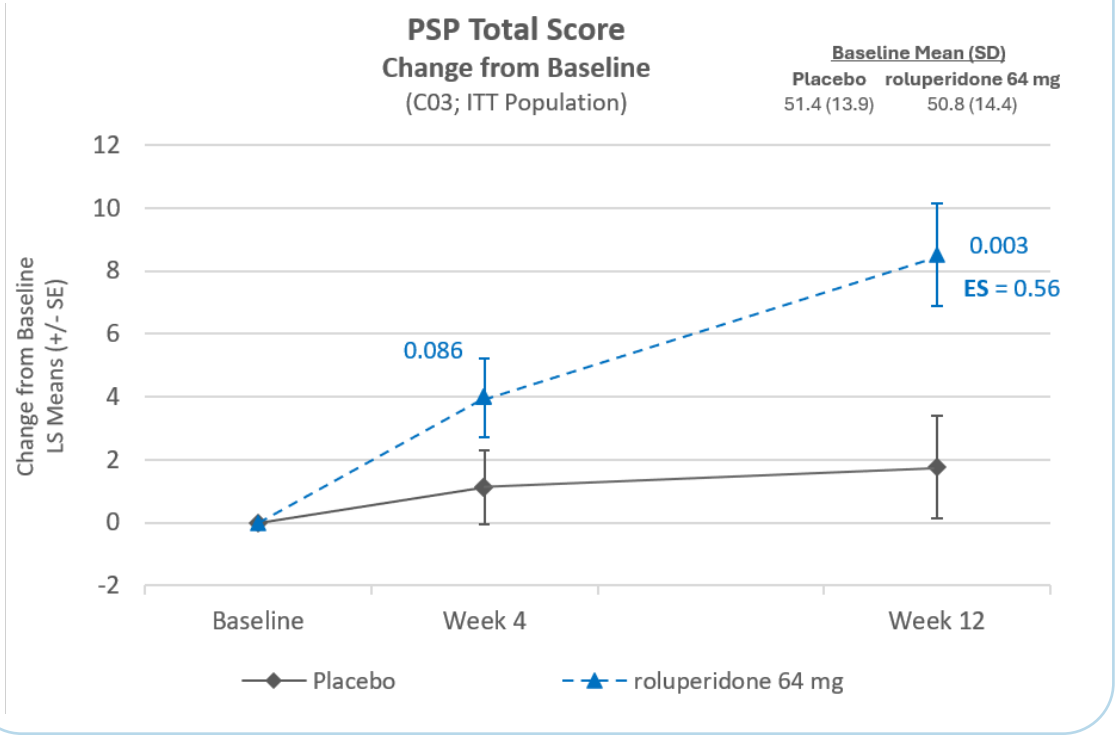
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[1] James, SH, … & Strauss, GP. Network intervention analysis indicates that roluperidone achieves its effect on negative symptoms of schizophrenia by targeting avolition. *European Neuropsychopharmacology* (2024)

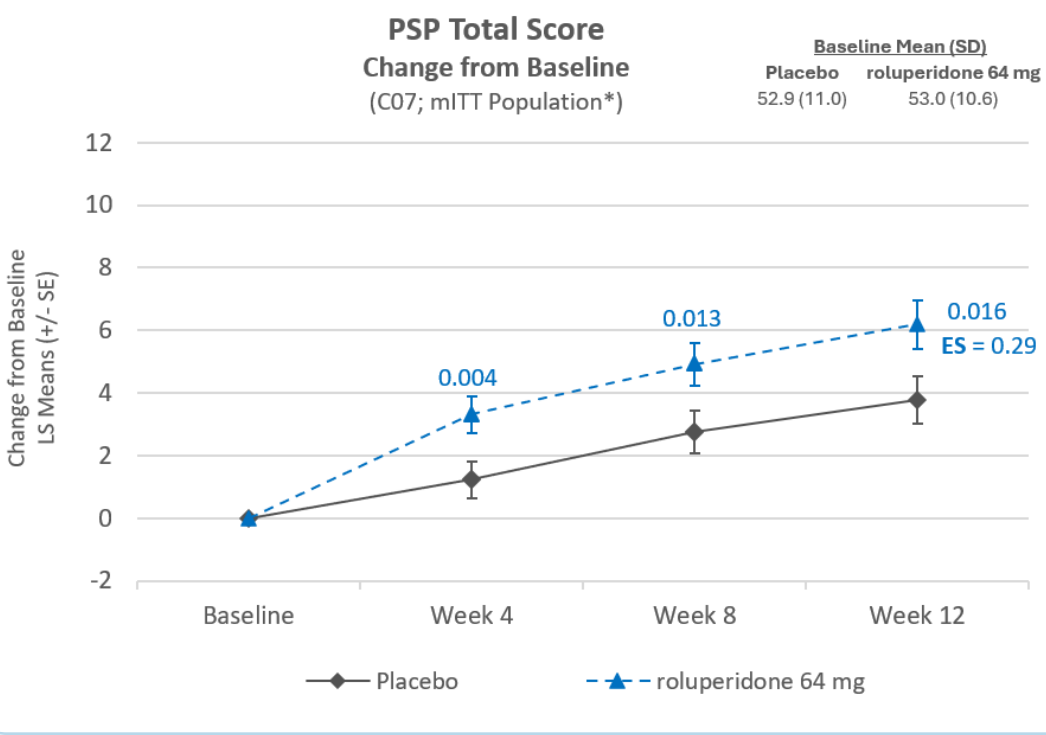
Why Does this Matter?
Functional Outcome Improves

C03 & C07 Studies: Personal and Social Performance (PSP) Score [1,2]

C03 Study



C07 Study

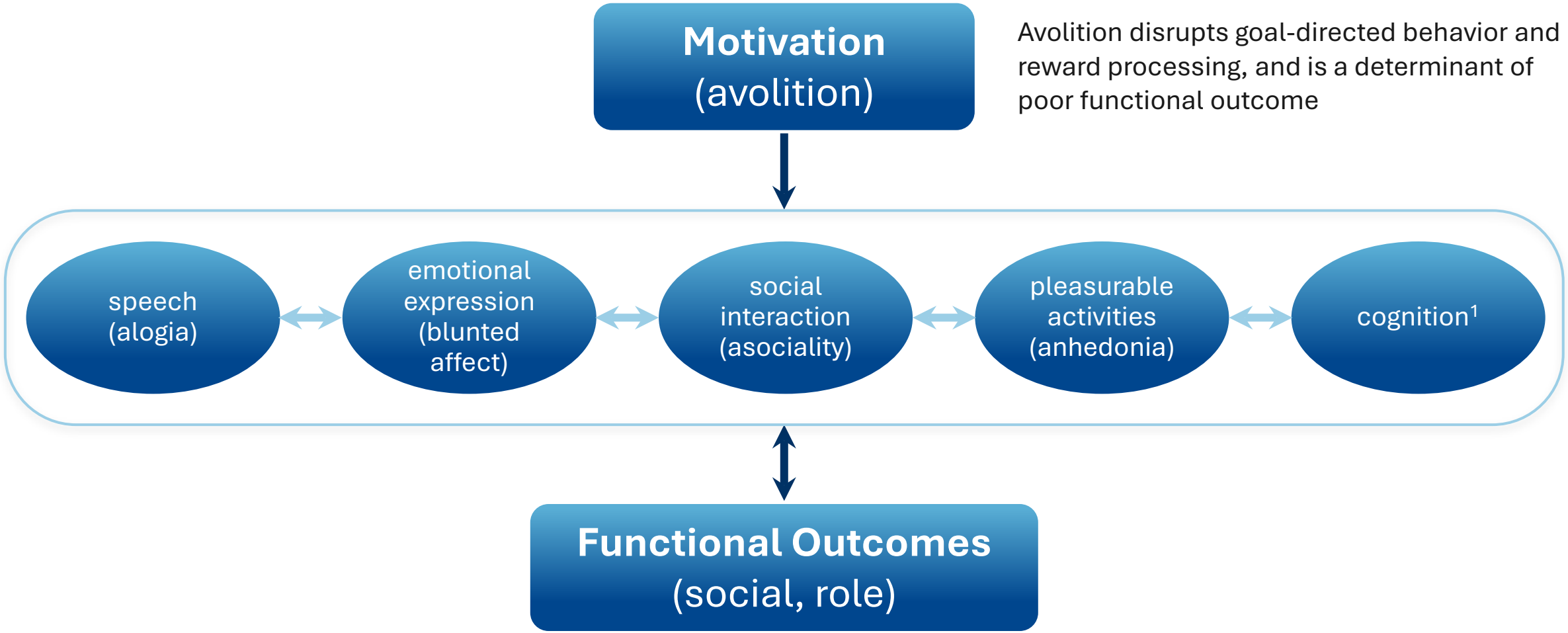


* mITT population (excludes 1 site for reasons of implausible data)

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[1]Rabinowitz et al. Personal and social adjustment effects of roluperidone in patients with schizophrenia and negative symptoms. *Schizophrenia Research* (2019);
[2]Rabinowitz et al. Long-term effects of Roluperidone on negative symptoms of schizophrenia. *Schizophrenia Research* (2023).

Targeting avolition improves entire constellation of negative symptoms & functional outcomes



Avolition disrupts goal-directed behavior and reward processing, and is a determinant of poor functional outcome

[1] Keefe, R et al. Cognitive Effects of MIN-101 in Patients with Schizophrenia and Negative Symptoms. *J.Clin.Psychiatry* (2018).

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Primary negative symptoms in the clinic



Brian Kirkpatrick, MD, MSPH
Peters Professor of Psychiatry
University of Arkansas for Medical Sciences

Clinical issues for patients with primary negative symptoms

- Who are these patients?
- Is monotherapy safe (or even beneficial for some patients)?
- What are the consequences of treating negative symptoms?

A distinctive group of patients

- There is extensive research on patients whose negative symptoms are not due to anxiety, depression, hallucinations, delusions, etc.
  - Predominant negative symptoms (the usual European term)
  - Primary negative symptoms
  - Deficit schizophrenia
- In a clinic they usually receive less attention than other outpatients
  - Hallucinations, delusions, disorganization of speech, & agitation are mild
    - These are features clinicians routinely assess
  - By definition, as a group they have less motivation (i.e., avolition)
  - They complain little and tend to stay if placed in a group home
  - In the absence of established treatments, clinicians are pessimistic about their prognosis
- Yet they have poorer function

Primary symptoms explain variance in function over & above other important symptoms: a 5-year longitudinal study

- Patients were rated for the presence/absence of primary negative symptoms
- Five years later they were assessed by other raters blind to the study hypothesis
- The primary/secondary categorization *made 5 years earlier* explained variance that was not accounted for by other symptoms

Measure	P value
Primary negative symptoms	0.017
Negative symptoms broadly defined	0.006
Hallucinations & delusions	0.026
Disorganized speech	>.001
Age	Nonsignificant
Sex	Nonsignificant
Age of onset	Nonsignificant

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Tek et al., A five-year followup study of deficit and nondeficit schizophrenia. *Schizophr Res*. 2001 Apr 30;49(3):253-60.

Monotherapy

- The fact that antipsychotics can decrease the number of relapses and hospitalizations in people with schizophrenia raises questions about the use of roluperidone as monotherapy
- As a group antipsychotics are associated with risk of:
  - weight gain and its consequences
  - movement side effects: tardive dyskinesia, restlessness, & stiffness
  - feeling sleepy during the day
  - hyperprolactinemia
- And antipsychotics do not improve primary negative symptoms and can worsen secondary negative symptoms

Patients who stop taking an antipsychotic have been studied for many years

- They have more relapses but serious consequences are rare
- Some patients will only take antipsychotics when they have increased symptoms
- Patients often have an increase in symptoms such as depression or anxiety before there is an increase in hallucinations, delusions, etc.
    - They and their loved ones often notice these early changes in time to stop the worsening of psychotic symptoms

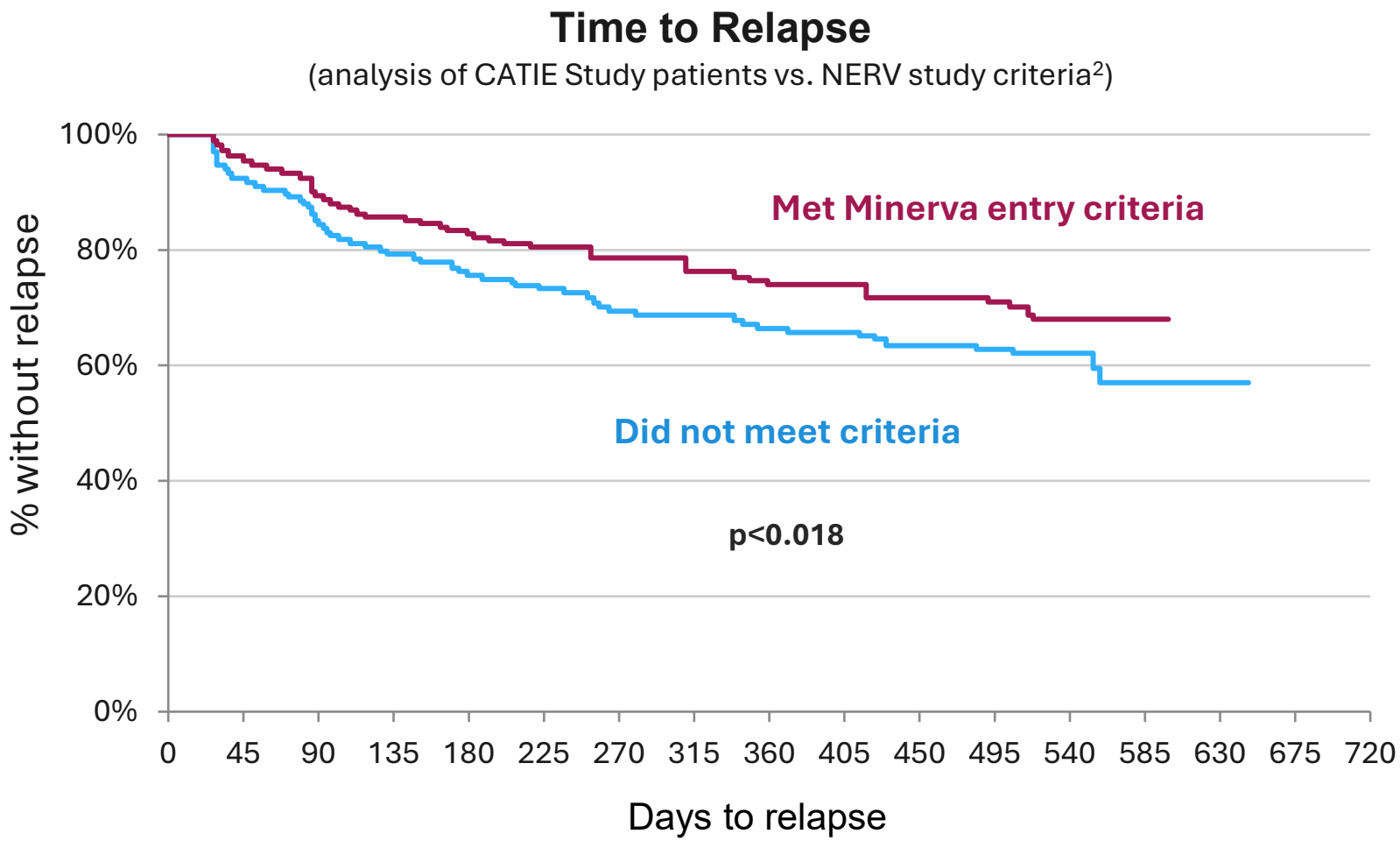
Patients meeting Minerva entry criteria have a low risk of relapse, independently of treatment

- The evidence:
  - the CATIE study, and Minerva's C03 & C07 studies
  - data from a meta-analysis of relapse rates for patients in studies of antipsychotic discontinuation
  - what is known about baseline symptoms and subsequent risk of relapse

Relapse in CATIE Study: analysis of patients who did/did not meet Minerva entry criteria

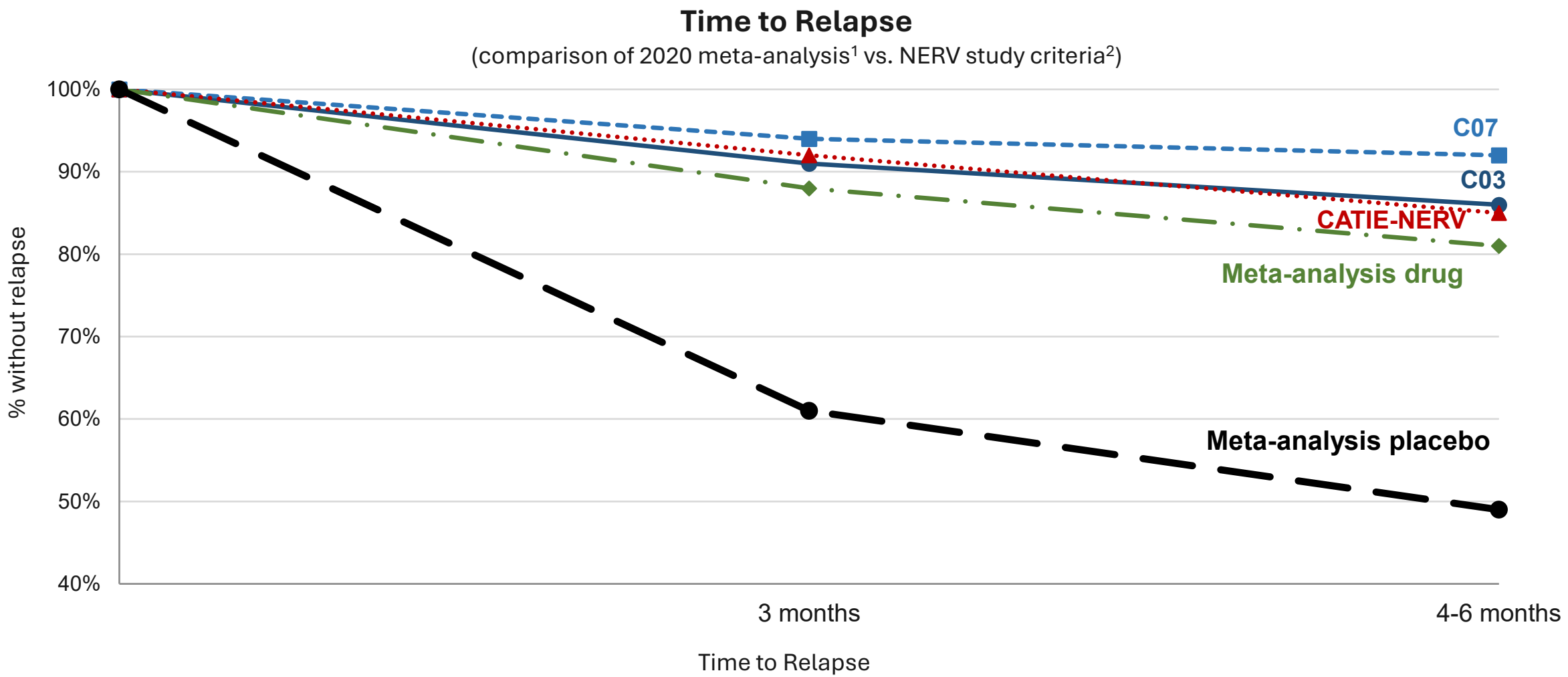
CATIE Study[1]

- 1,493 schizophrenia patients recruited from 47 US sites
- Randomly assigned to 1 of 5 antipsychotics
- Followed longitudinally



[1]Lieberman JA, et al. Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. *NEJM* (2005); [2]Source: Minerva Neurosciences (data on file); **NERV**: Minerva Neurosciences

Relapse in patients meeting Minerva entry criteria: comparison to a meta-analysis of antipsychotic trials



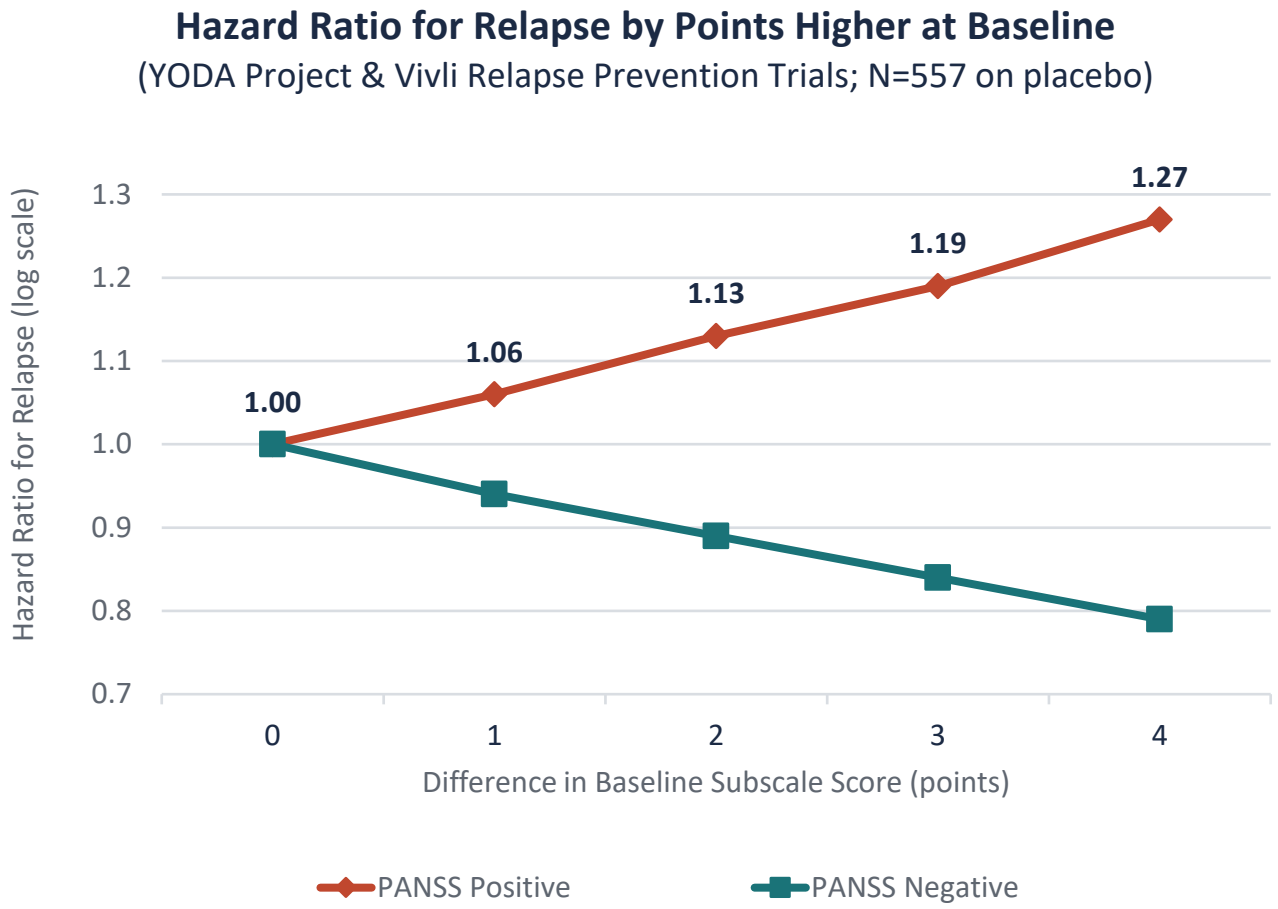
[1]Ceraso A, Lin JJ, et al., Maintenance treatment with antipsychotic drugs for schizophrenia. Cochrane Database Syst Rev. (2020 Aug), reviewing 75 randomized controlled trials involving 9,145 participants comparing antipsychotic medication with placebo; [2]Source: Minerva Neurosciences (data on file); **NERV**: Minerva Neurosciences

Baseline positive and negative symptoms predict relapse in opposing directions among placebo-treated schizophrenia patients in double-blind studies (YODA & Vivli)

The Minerva entry criteria define a group with low positive symptoms and high negative symptoms.

Low-positive, high-negative symptom profiles are less likely to relapse.

Given this, patients in Minerva's clinical studies *should have* a low risk of relapse. It would have been surprising it they hadn't.



Rabinowitz et al, Factors predicting symptom stability without antipsychotic treatment in schizophrenia: analysis of 557 patients on placebo for at least 6 months. Presented at European College of Neuropsychopharmacology (ECNP conference Oct. 2026, Munich. PS01-1230). Other source: Minerva Neurosciences.

The interpretation and reporting of research using this data do not represent the views of the YODA Project or Vivli, Inc.

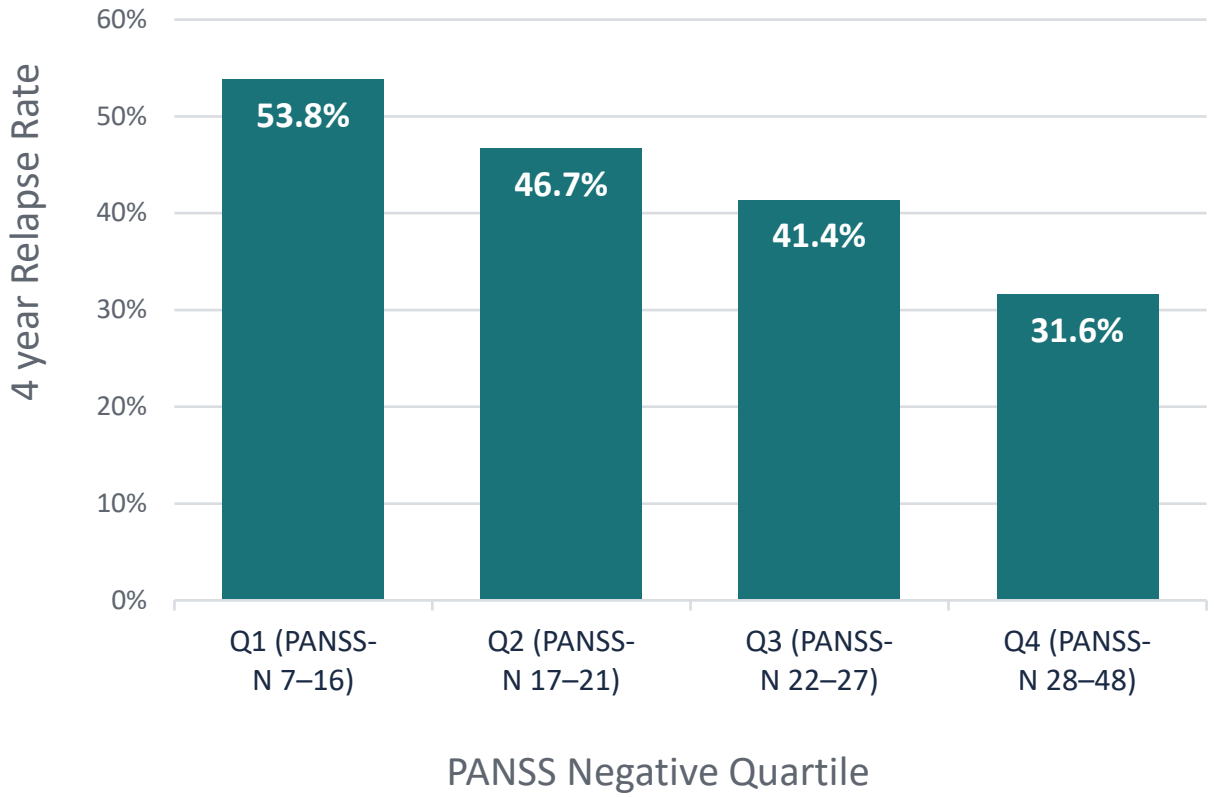
Baseline negative symptom severity and relapse risk in an Italian cohort

Four-year follow-up in 24 university psychiatric clinics and mental health departments.[1]

4-year relapse risk fell steadily as baseline negative symptoms rose.

A high-negative baseline profile with a negative symptoms profile consistent with C03 and C07 identifies patients who are less likely to have a relapse.

Adjusted 4-yr Relapse Rate by Baseline PANSS Negative Quartile
(NIRP 4-yr Follow-up)



[1] NIRP Study: Mucci A, Galderisi S, et al. Factors associated with real-life functioning in persons with schizophrenia in 4-year follow-up study of Italian Network for Research on Psychoses. *JAMA Psychiatry*. (2021).

Source: Minerva Neurosciences. The interpretation and reporting of research using NIRP Study data do not necessarily represent the views of its authors. **OR** = Odds Ratio.

The evidence on relapse: what does it mean?

- The consistently lower relapse risk in this population across years, national borders and various definitions of relapse (including hospitalization) provides evidence for
  - the existence and validity of those with this symptom profile
  - for this group roluperidone has a reasonable risk/benefit ratio

Monotherapy with roluperidone is an example of precision medicine.

The long-term effects of treatment

- Many of these patients:
  - Have had years of relative isolation and poor function
  - May not have confidence or skills with regard to self-care, relationships, and employment
- Roluperidone patients have shown improvement in function (PSP) in the C03 & C07 Studies
- An important consequence of successful treatment of their negative symptoms will be that they are able to respond more to evidence-based psychosocial treatments.
  - Which should lead to further improvement.

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PSP: Personal and Social Performance Scale

New analyses strengthening uniqueness of roluperidone in treating negative symptoms



Remy Luthringer, PhD

Executive Chairman & Chief Executive Officer
Minerva Neurosciences, Inc.

NEW ANALYSES

- Bayesian Methodology Applied to C03 & C07 Studies
- Global Statistical Test (GST)
- Responder Analysis Across Endpoints

Bayesian methodology applied to C03 & C07 Studies

FDA Guidance

FDA's January 2026 draft guidance on Bayesian methodology encourages combining an earlier trial with a new confirmatory trial when the two are similar enough to justify it.[1]

When applying Bayesian methodology to the C03 & C07 Studies, the posterior probability of superiority needs to be **>98.75%**

NSFS (64 mg)

97.9% → **99.4%**

PSP (64 mg)

97.8% → **98.8%**

C07 Study alone
(slightly below 98.75% bar)

Bayesian Analysis
(20% borrowing)

Only modest borrowing needed to establish superiority

- Borrowing 20% of C03 Study (less than 50 patients of the overall 244 patients)

[1] Use of Bayesian Methodology in Clinical Trials of Drug and Biological Products (draft guidance), January 2026.

C03 (n = 244); C07 (n = 496); **NSFS:** Marder Negative Symptoms Factor Score; **PSP:** Personal and Social Performance scale. Source: Minerva Neurosciences.

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Global Statistical Test (GST)

Global Statistical Test

GST combines endpoints into a single test while correcting for correlation, so that redundant measures do not inflate the result.[1]

GST Analysis

Roluperidone 64mg vs. placebo

GST Results (NSFS +PSP)	**p-value**
C03 alone	<.0001
C07 alone	.0095
Integrated C03 & C07	.0001

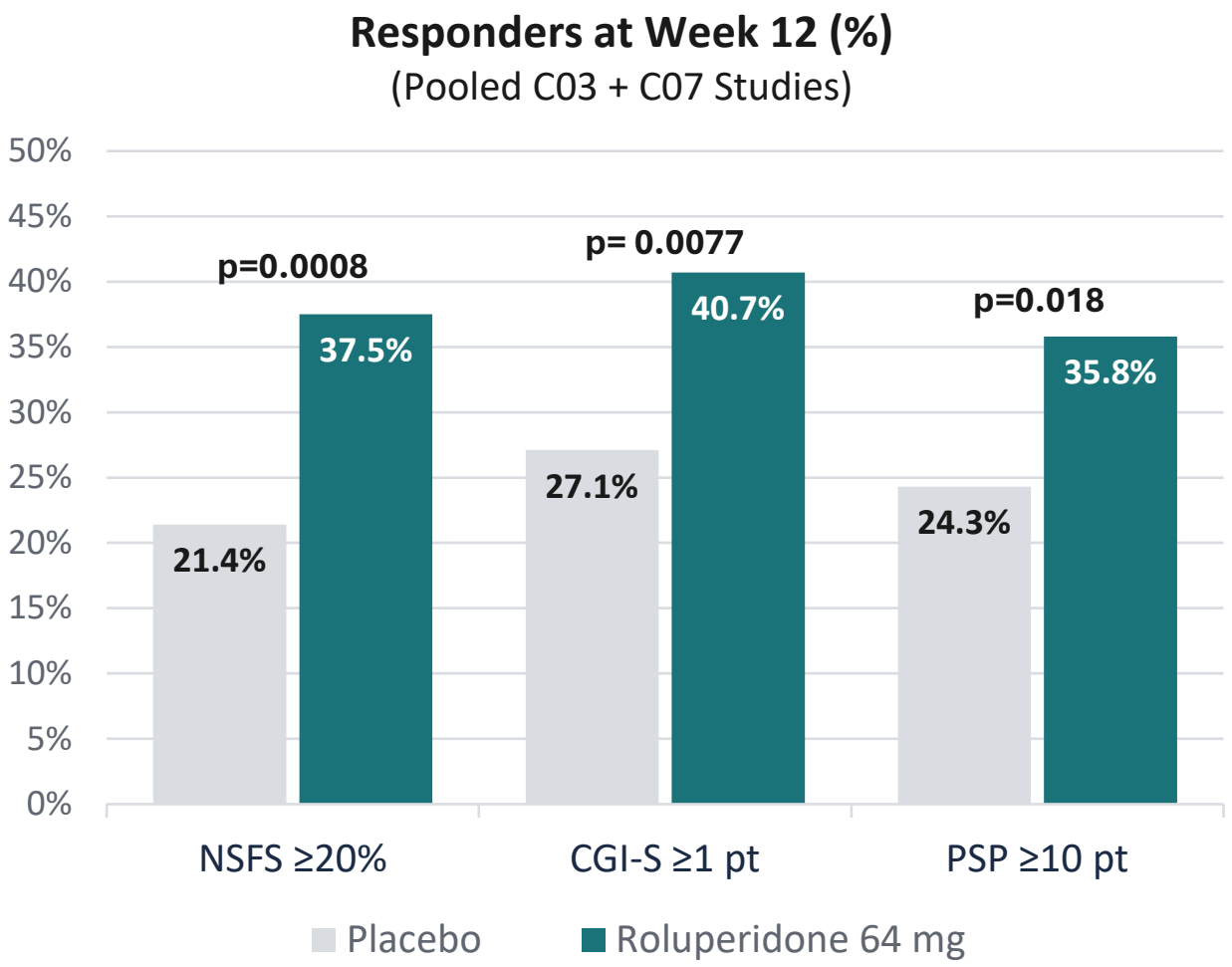
Results within each study (and integrated) support broad, consistent efficacy of roluperidone on negative symptoms which allows improvement of functioning

[1] O'Brien PC. Procedures for comparing samples with multiple endpoints. *Biometrics*. 1984;40(4):1079-1087.

C03 (n = 244); C07 (n = 496); **NSFS:** Marder Negative Symptoms Factor Score; **PSP:** Personal and Social Performance scale. Source: Minerva Neurosciences.

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Responder Analysis Across Endpoints



NUMBER NEEDED TO TREAT

7	8	9
NSFS ≥20%	CGI-S ≥1 pt	PSP ≥10 pt

Meaningful across three independent anchors

Higher responder rates than placebo on symptoms (**NSFS**), clinician global (**CGI-S**), and functioning (**PSP**) (RR 1.47–1.75).

NNTs of 7–9 fall within the range of approved antipsychotics (NNT 5) and antidepressants (NNT 8); comparisons are indirect.

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Pooled analysis of C03 + C07 studies, roluperidone 64 mg vs placebo,12-week completers. **NSFS:** Marder Negative Symptoms Factor Score; **CGI-S**: Clinical Global Impression - Severity of illness; **PSP:** Personal and Social Performance scale. Source: Minerva Neurosciences. Source: Minerva Neurosciences.

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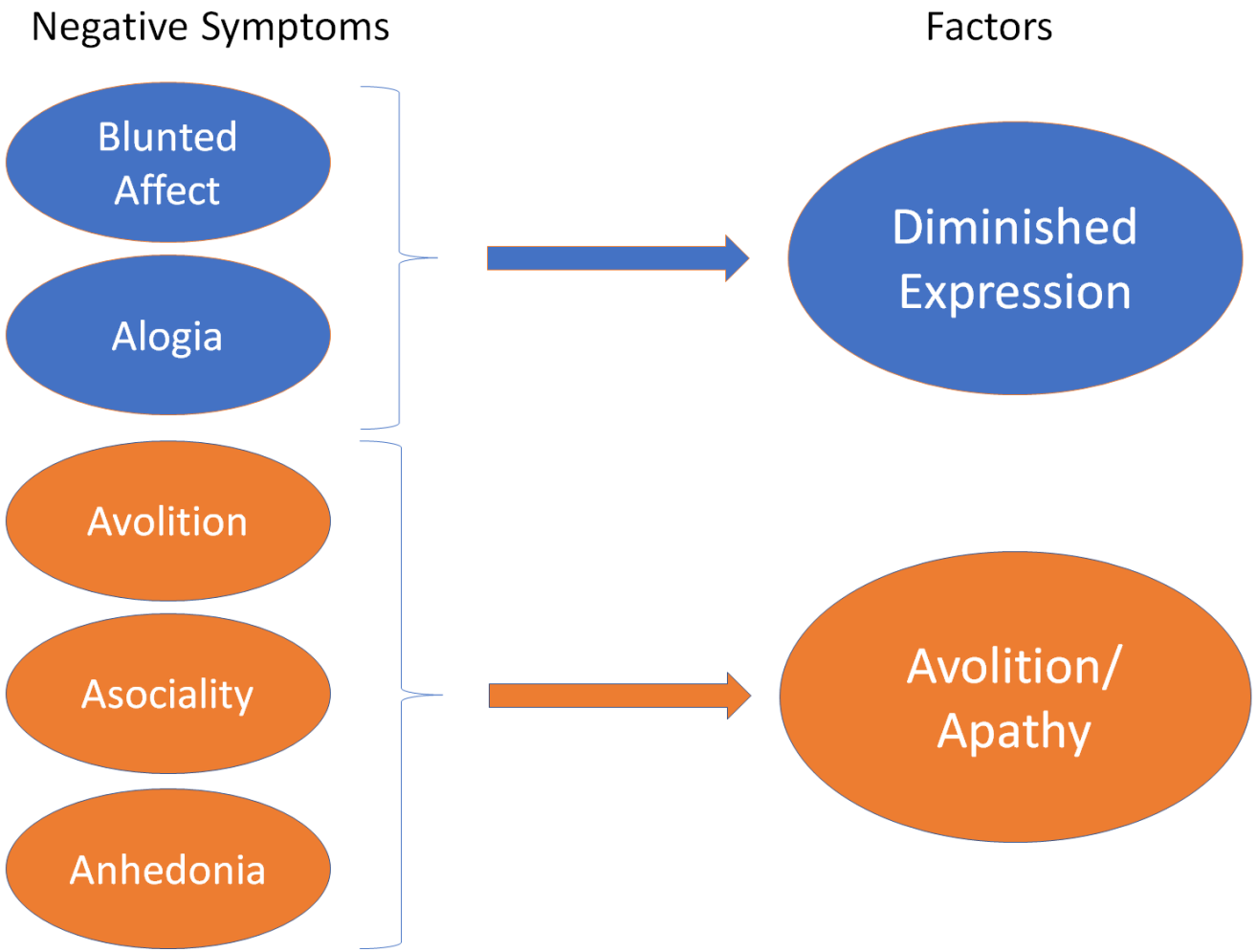
Transdiagnostic nature of negative symptoms supporting the promise of addressing unmet needs beyond schizophrenia



Christoph Correll, MD

Clinical Professor of Psychiatry and Molecular Medicine
The Donald and Barbara Zucker School of Medicine at Hofstra University
Professor and Chair of Department of Child and Adolescent Psychiatry
Charite University Medicine, Berlin

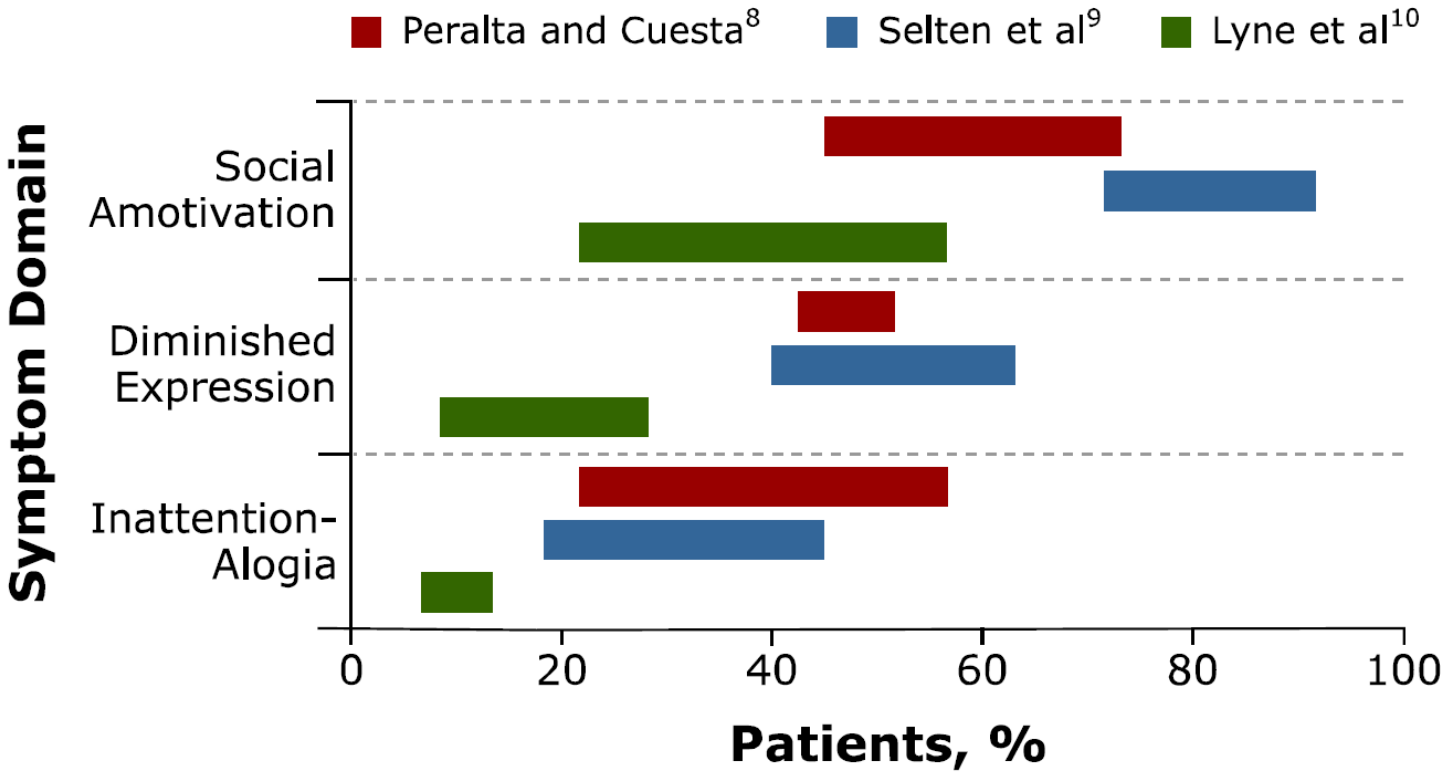
Key Negative Symptom Constructs in Schizophrenia



Correll CU and Schooler NR, *Neuropsychiatr Dis Treat.* 2020 Feb 21;16:519-534.

Negative Symptoms: How Common are They?

- According to 3 studies, social amotivation is the most prevalent negative symptom, followed by diminished expression, and then inattention-alogia



Correll CU. *J Clin Psychiatry*. 2013;74(2):e04.

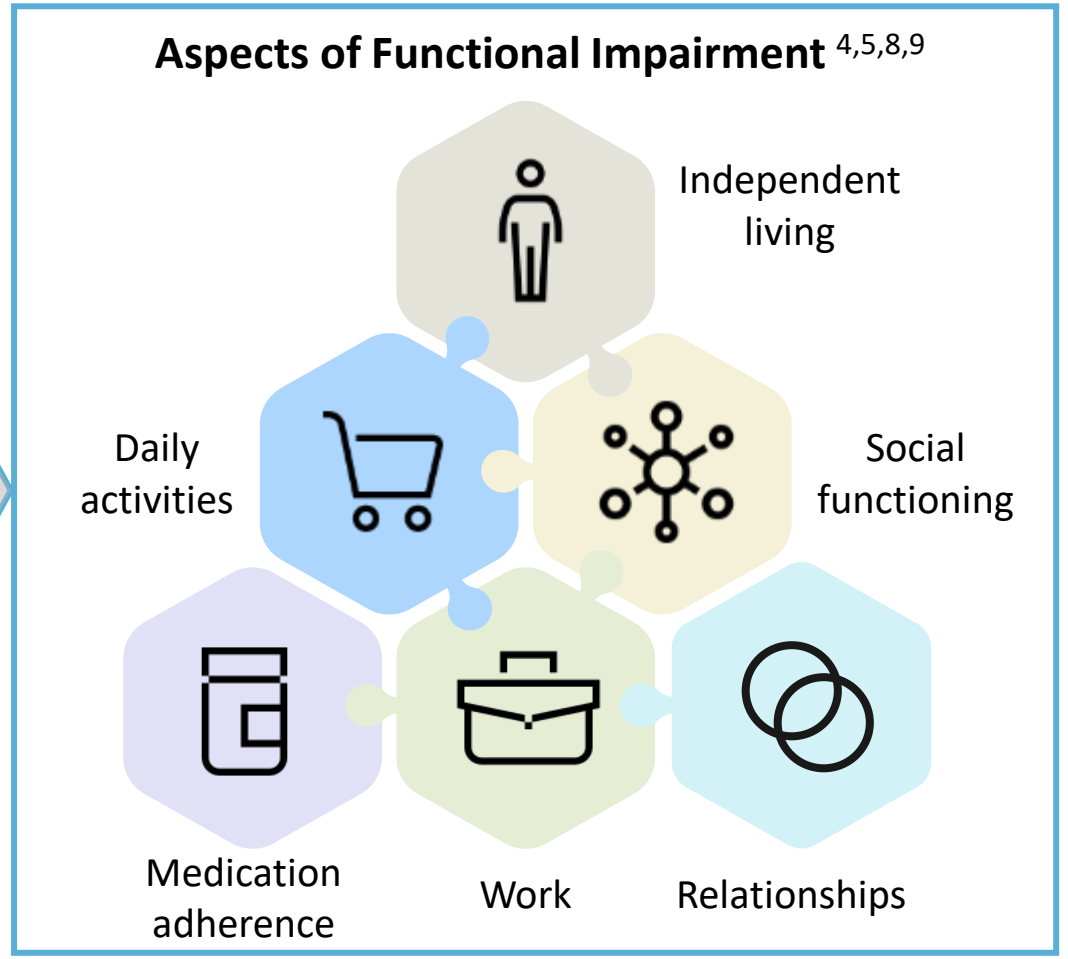
See www.cmeinstitute.com/psychlopedia/Documents/psychosis/5cpem/sec3/psy5-3_AV2.htm. Accessed August 10, 2017.

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Negative Symptoms in Schizophrenia Predict Real-world Functioning[1-4]

Negative symptoms

- **Predict poorer outcomes and long-term disability**[4,5,6]
- **Affect the *likelihood* of performing everyday skills**[7]



[1]Fervaha G, et al. *Acta Psychiatr Scand*. 2014;130:290-299; [2]Bowie CR, et al. *Am J Psychiatry*. 2006;163:418-425; [3]Quinlan T, et al. *Schizophr Res*. 2014;157:182-181; [4]Correll CU, Schooler NR. *Neuropsychiatr Dis Treat*. 2020;16:519-534; [5]Loch AA. *Front Psychiatry*. 2019;10:328; [6]Harvey PD, et al. *J Exp Psychopathol*. 2019;1-20; [7]Harvey PD, et al. *Schizophr Bull*. 2006;32(2):250-258; [8]Bowie CR, Harvey PD. *Neuropsychiatr Dis Treat*. 2006;2:531-536; [9]McCutcheon RA, et al. *Mol Psychiatry*. 2023;28:1902-1918.

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Interaction Between Cognitive and Negative Symptoms Converging on Functional Outcomes

- Both amotivation/apathy and cognitive psychopathology independently contribute to longitudinal **functional outcomes** among patients with schizophrenia
  - Quality of life, relationships, work performance, social functioning
- Cognitive performance affects patients' **ability** to perform everyday skills (**functional capacity**)
- Negative symptoms affect patients' **likelihood** of performing these skills (**functional performance**)

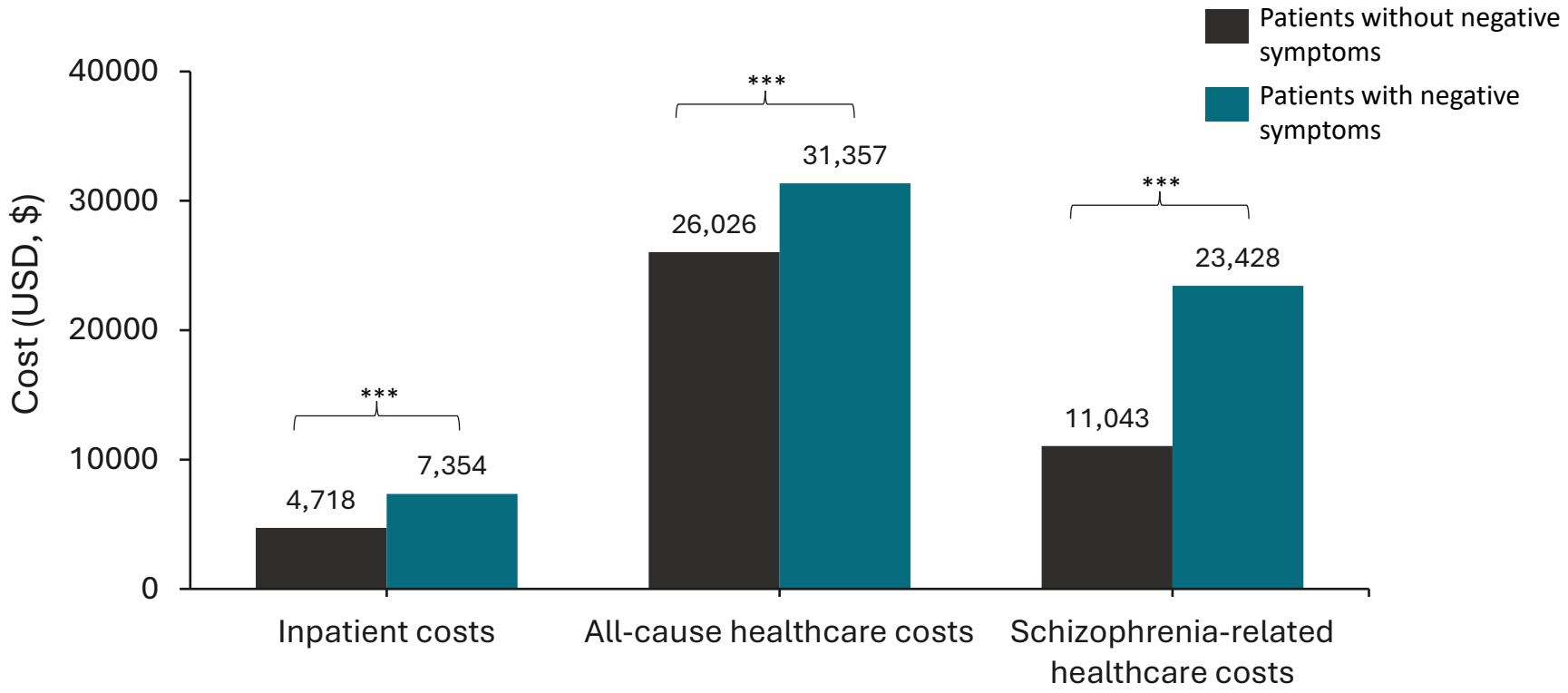
Fervaha G, et al. *Acta Psychiatr Scand*. 2014;130(4):290-299. Ritsner MS, et al. *J Nerv Ment Dis*. 2011;199(11):845-853. Strauss GP, et al. *Schizophr Res*. 2011;128(1-3):117-123. Bowie CR, et al. *Am J Psychiatry*. 2006;163(3):418-425.

Negative Symptoms in Schizophrenia are Correlated with Higher Healthcare Costs

Data from electronic health records

for 79,326 adults with diagnosed schizophrenia

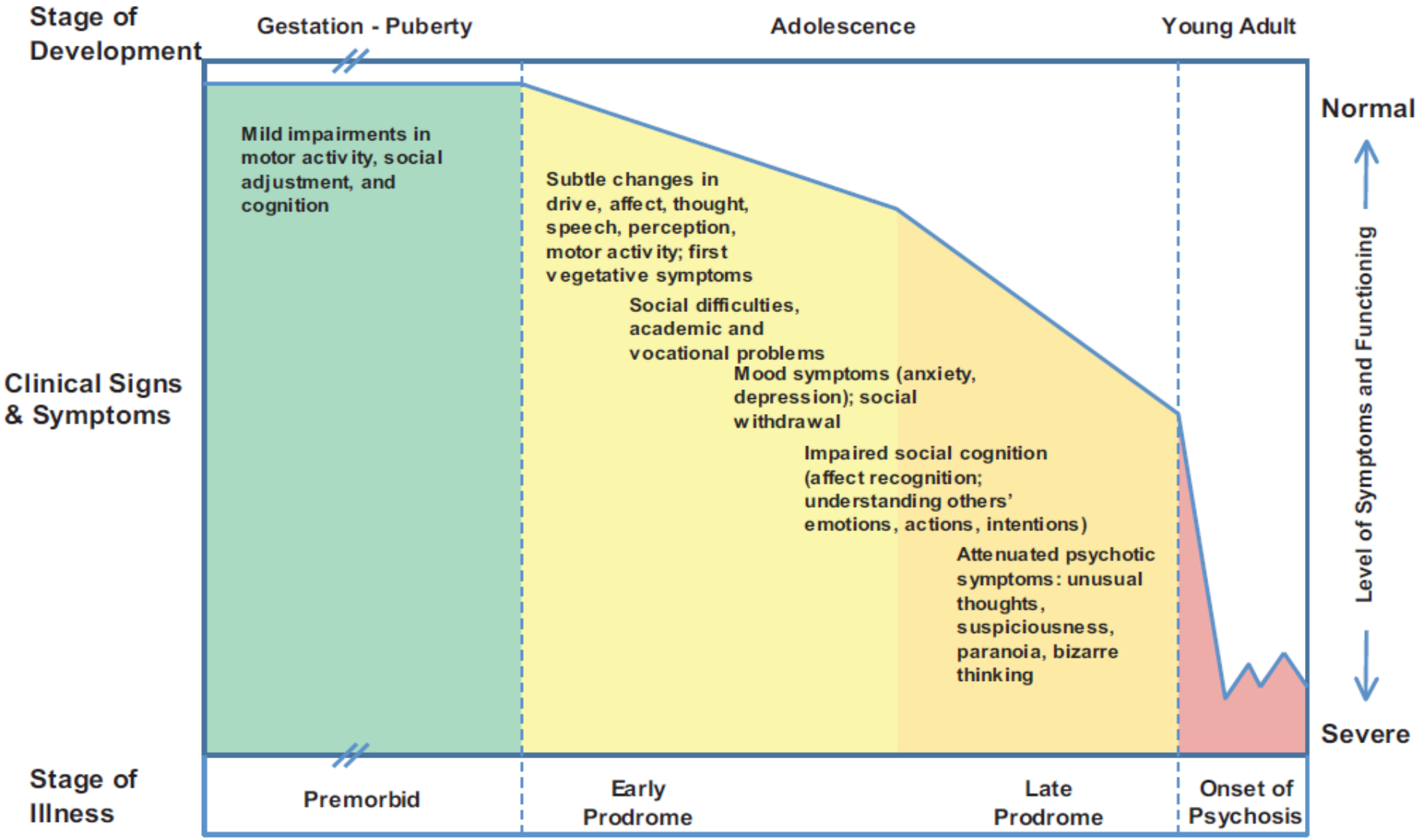
Patients with negative symptoms (n=1975) had **significantly higher healthcare costs** than patients without negative symptoms (n=9318)



*** *P*<.001.

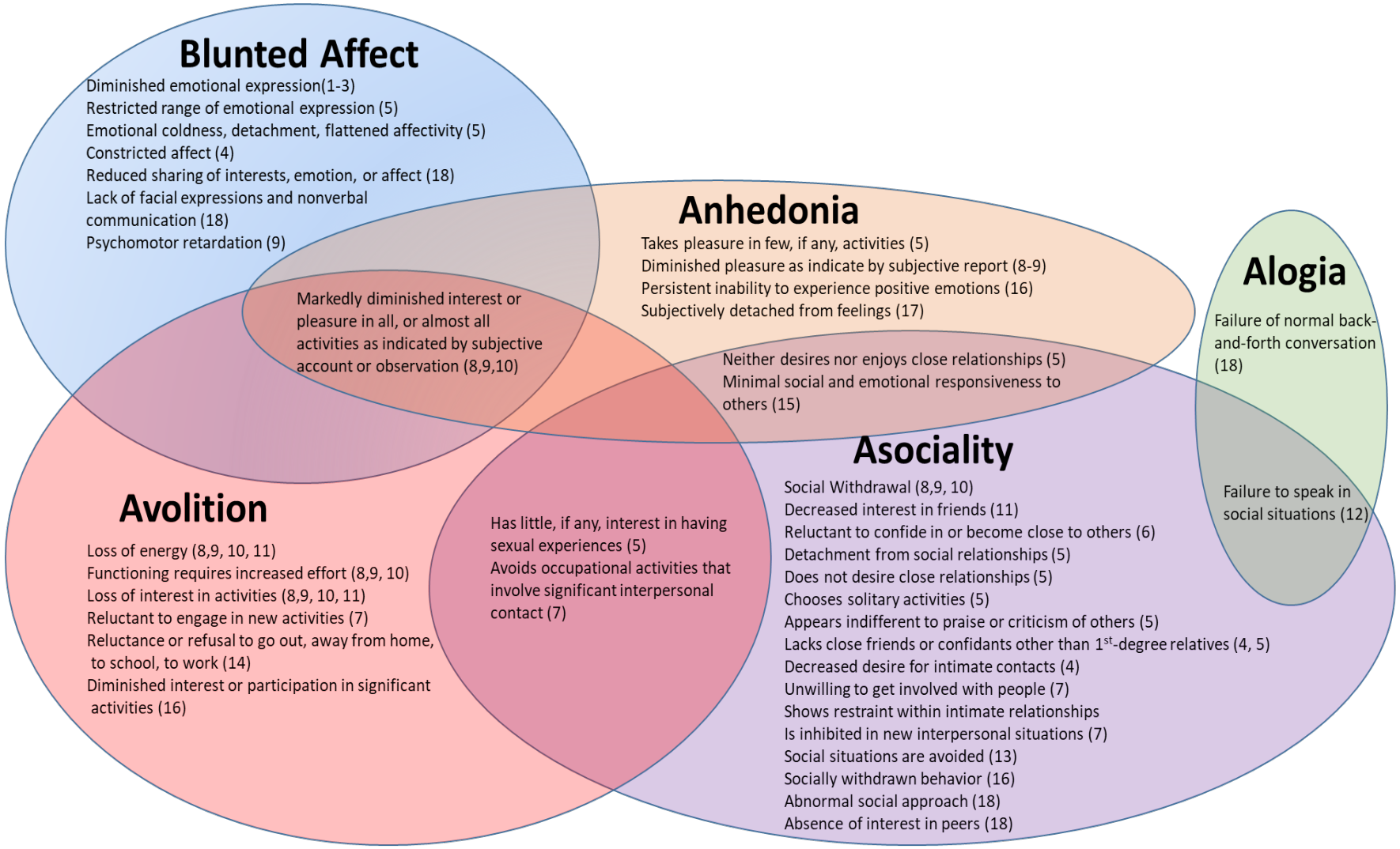
Vaccaro J, et al. *Schizophr Bull*. 2026 Mar 7;52(2):sbaf073.

Early Identification and Prevention: The Role and Place of Negative Symptoms



Addington, J., & Heinssen, R. (2012). Prediction and prevention of psychosis in youth at clinical high risk. *Annual review of clinical psychology*, *8*, 269-289.

Negative Symptoms Occur Outside of Schizophrenia - we just don't call them that



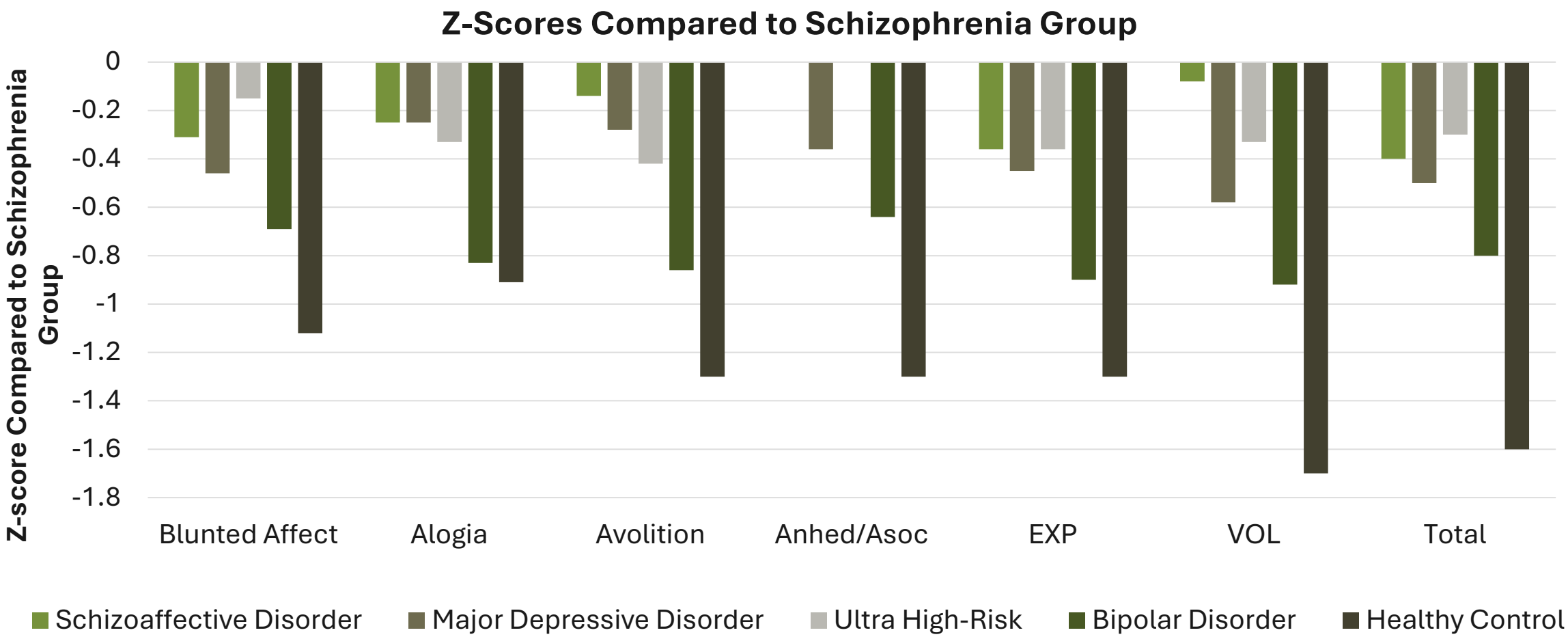
DSM-5 Disorders with Negative Symptoms

1. Schizophrenia
2. Schizoaffective Disorder
3. Schizophreniform Disorder
4. Schizotypal Personality Disorder
5. Schizoid Personality Disorder
6. Paranoid Personality Disorder
7. Avoidant Personality Disorder
8. Bipolar Disorder (I and II)
9. Major Depressive Disorder
10. Persistent Depressive Disorder (Dysthymia)
11. Premenstrual Dysphoric Disorder
12. Selective Mutism
13. Social Anxiety Disorder
14. Separation Anxiety Disorder
15. Reactive Attachment Disorder
16. Posttraumatic Stress Disorder
17. Depersonalization/Derealization Disorder
18. Autism Spectrum Disorder
19. Neurocognitive Disorders

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Strauss, GP & Cohen, AS. A transdiagnostic review of negative symptom phenomenology and etiology. *Schizophrenia bulletin*. (2017) *43*(4), 712-719.

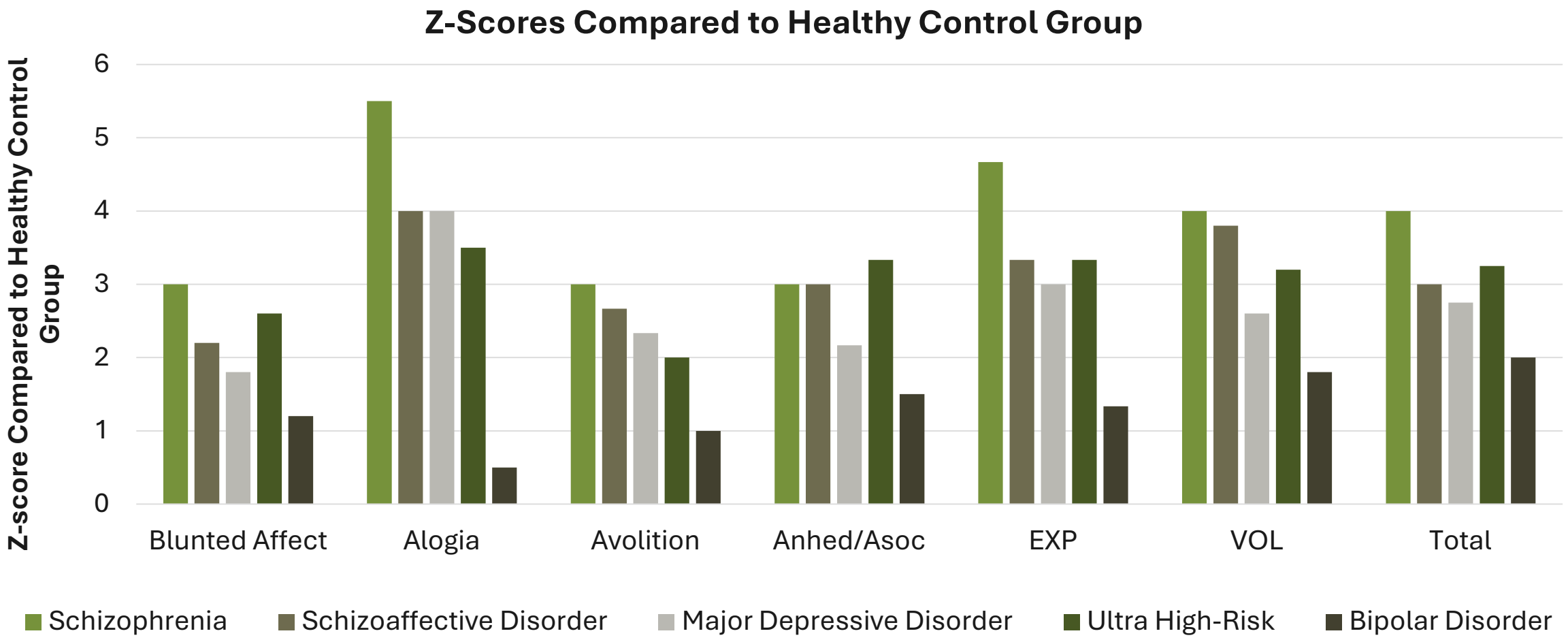
How severe are negative symptoms when they occur during the psychosis prodrome and outside of schizophrenia?



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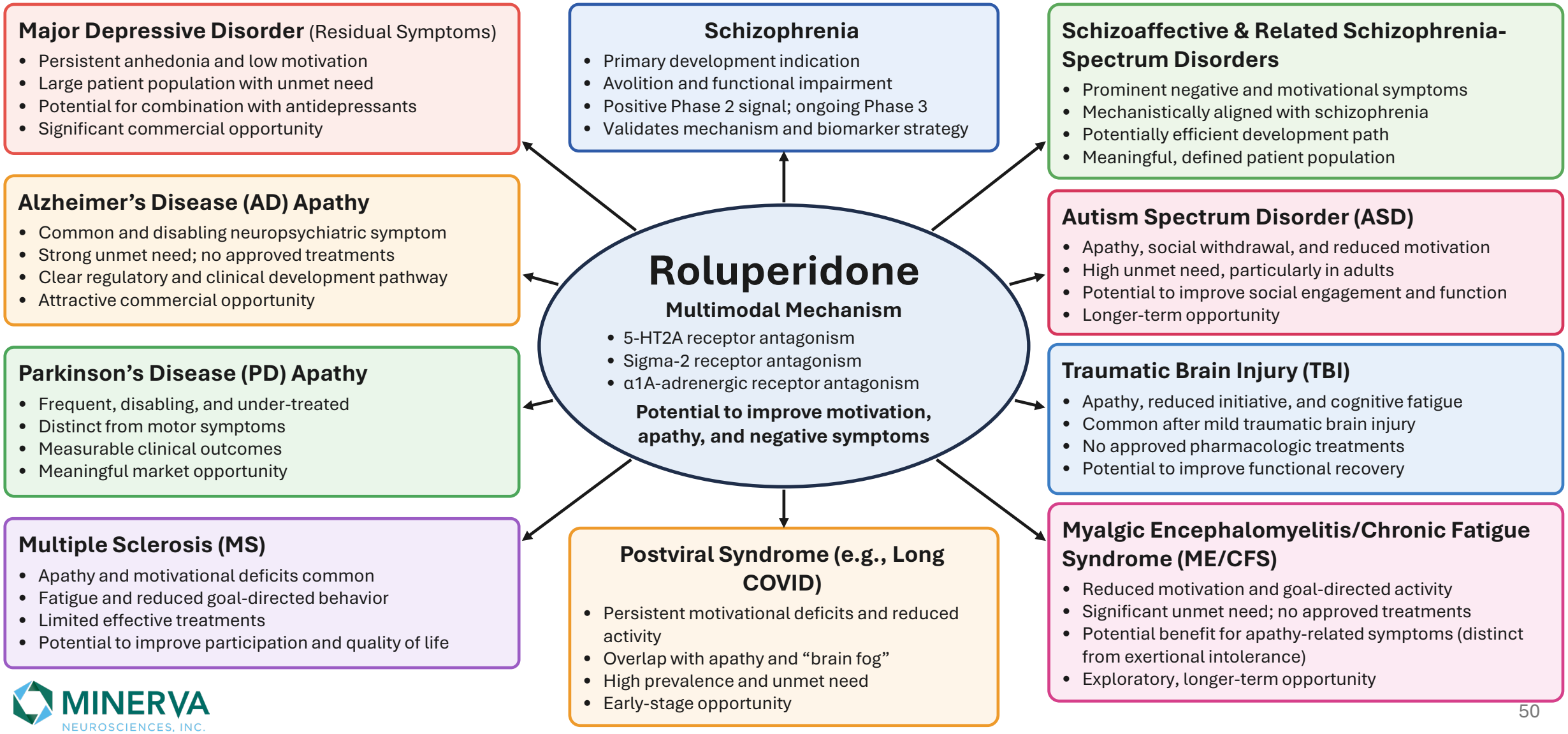
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Transdiagnostic opportunities for roluperidone



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Market Opportunity



Remy Luthringer, PhD

Executive Chairman & Chief Executive Officer
Minerva Neurosciences, Inc.

~900,000 US Adults Fit the Roluperidone Target Profile

~3.4M

Adults with schizophrenia, U.S.

1.17% age-adjusted prevalence[1]

~2.2M

Diagnosed schizophrenia prevalence, U.S.[2]

Estimated to increase to ~2.5M by 2035[2]

~1.3M

Prominent or predominant, clinically relevant negative symptoms

~60% of treated patients[3]

~900k

Stable patients: target patients for roluperidone

~68.9% of diagnosed schizophrenia patients have stable positive symptoms[4]

[1]Krasa et al., National and State Societal Costs of Schizophrenia in the US in 2024. *JAMA Psychiatry* (2026); [2]Clarivate Schizophrenia Disease Landscape & Forecast (Major Markets) (2026); [3] Correll CU, Schooler NR. Negative Symptoms in Schizophrenia: A Review and Clinical Guide for Recognition, Assessment, and Treatment. *Neuropsychiatr Dis Treat*. (2020); [4] Starzer, M., Hansen, H.G., Hjorthøj, C., Albert, N., Nordentoft, M. and Madsen, T. (2023), 20-year trajectories of positive and negative symptoms after the first psychotic episode in patients with schizophrenia spectrum disorder: results from the OPUS study. World Psychiatry,

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A multi-billion-dollar category where negative symptoms get $0 despite massive unmet need

~$7.1B

US schizophrenia drugs market, 2025

Growing at ~4.5% CAGR[1]

$0

Approved treatments for negative symptoms in the US

>$2B

Roluperidone peak annual US net sales potential as the first approved negative-symptoms therapy[2]

Today's antipsychotics, including newer entrants, are labeled for schizophrenia broadly and primarily control positive symptoms.

Negative symptoms persist after positive symptoms stabilize and drive long-term disability; physicians rank them a top unmet need.

Roluperidone is the only late-stage candidate targeting primary negative symptoms directly.

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1. Clarivate Schizophrenia Disease Landscape & Forecast (Major Markets), 2026. 2. Based on estimates including Minerva Neurosciences estimates of TAM, market share, pricing and adoption including input from 2024 Payer survey conducted by Lumanity Inc.

Summary: The Minerva Confluence

Right pharmacology and MOA

- **Only drug to date** to show a significant, clinically relevant improvement
- Specific to **primary negative symptoms** of schizophrenia
- **Label expansion** opportunities for multiple indications beyond schizophrenia

Right patient profile

- Clinically relevant population with predominant and **impairing negative symptoms**
- Moderate to severe negative symptom patients, as shown in C03, C07, and several other studies, have a relatively **low risk of relapse**

Right phase 3 trial design

- **Previous experience** with two statistically significant (one nominally) trials
- **FDA alignment** on ongoing Phase 3 trial
- **Ongoing 'high touch'** confirmatory Phase 3 trial increases probability of success

Right moment

- **Broad awareness** of unmet need in psychiatry community
- Backed by **world-class investors**
- Near-term opportunity to be the first treatment for negative symptoms of schizophrenia

Q&A

A new approach to treating the unmet needs of schizophrenia patients

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Roluperidone for negative symptoms of schizophrenia

Clinical data that matters