

# The New and the Old of Newer is Better

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May 29, 2025  
ASCP

# Agenda

- What does “better” mean?
- Are psychedelics better?
- How do we evaluate better?
- How are we trying to get better?

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# MDMA for PTSD

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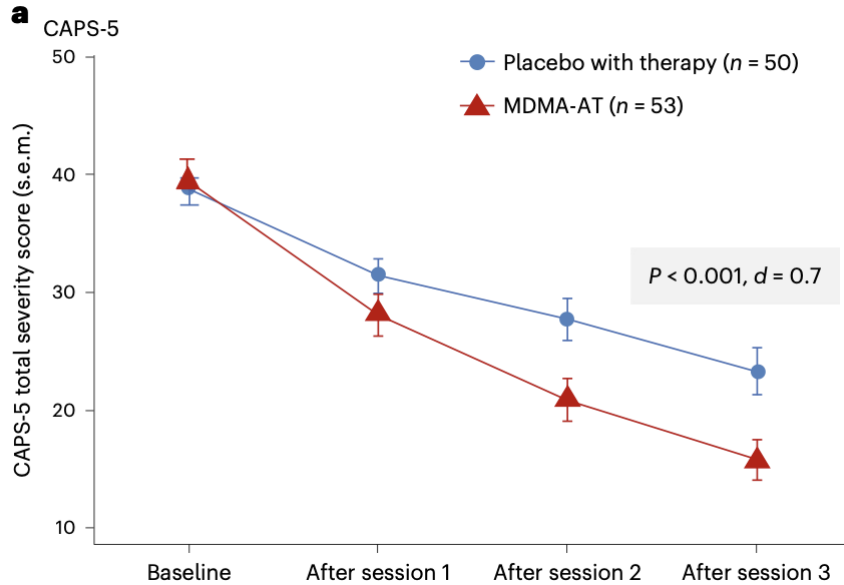
Article | [Open access](#) | Published: 14 September 2023

## **MDMA-assisted therapy for moderate to severe PTSD: a randomized, placebo-controlled phase 3 trial**

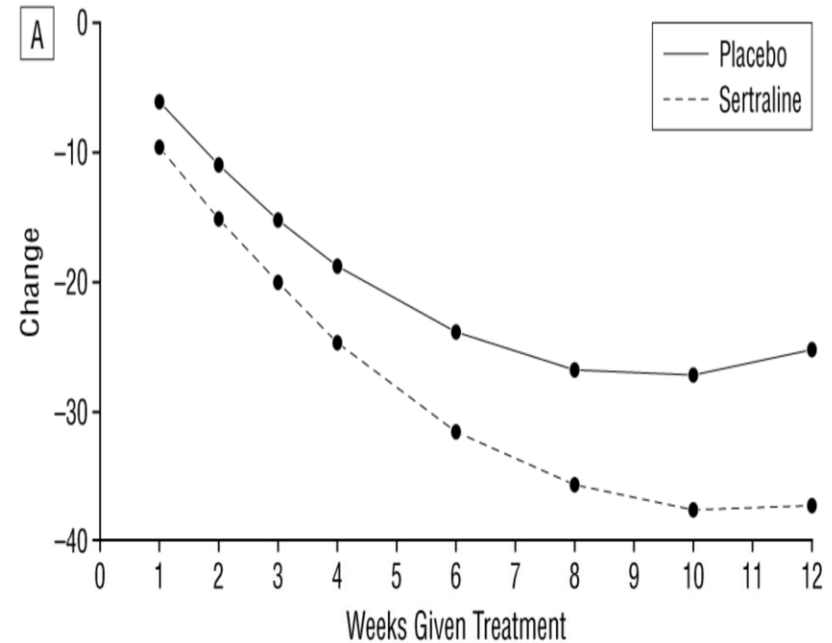
[Jennifer M. Mitchell](#) , [Marcela Ot'alora G.](#), [Bessel van der Kolk](#), [Scott Shannon](#), [Michael Bogenschutz](#), [Yevgeniy Gelfand](#), [Casey Paleos](#), [Christopher R. Nicholas](#), [Sylvestre Quevedo](#), [Brooke Balliett](#), [Scott Hamilton](#), [Michael Mithoefer](#), [Sarah Kleiman](#), [Kelly Parker-Guilbert](#), [Keren Tzarfaty](#), [Charlotte Harrison](#), [Alberdina de Boer](#), [Rick Doblin](#), [Berra Yazar-Klosinski](#) & [MAPP2 Study Collaborator Group](#)

[Nature Medicine](#) **29**, 2473–2480 (2023) | [Cite this article](#)

# MDMA



# Sertraline



Original Article

May 2001

## Multicenter, Double-blind Comparison of Sertraline and Placebo in the Treatment of Posttraumatic Stress Disorder

Jonathan R. T. Davidson, MD; Barbara O. Rothbaum, PhD; Bessel A. van der Kolk, MD; et al.

> Author Affiliations | Article Information

Arch Gen Psychiatry. 2001;58(5):485-492. doi:10.1001/archpsyc.58.5.485

# Psilocybin for Depression



The NEW ENGLAND  
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ORIGINAL ARTICLE



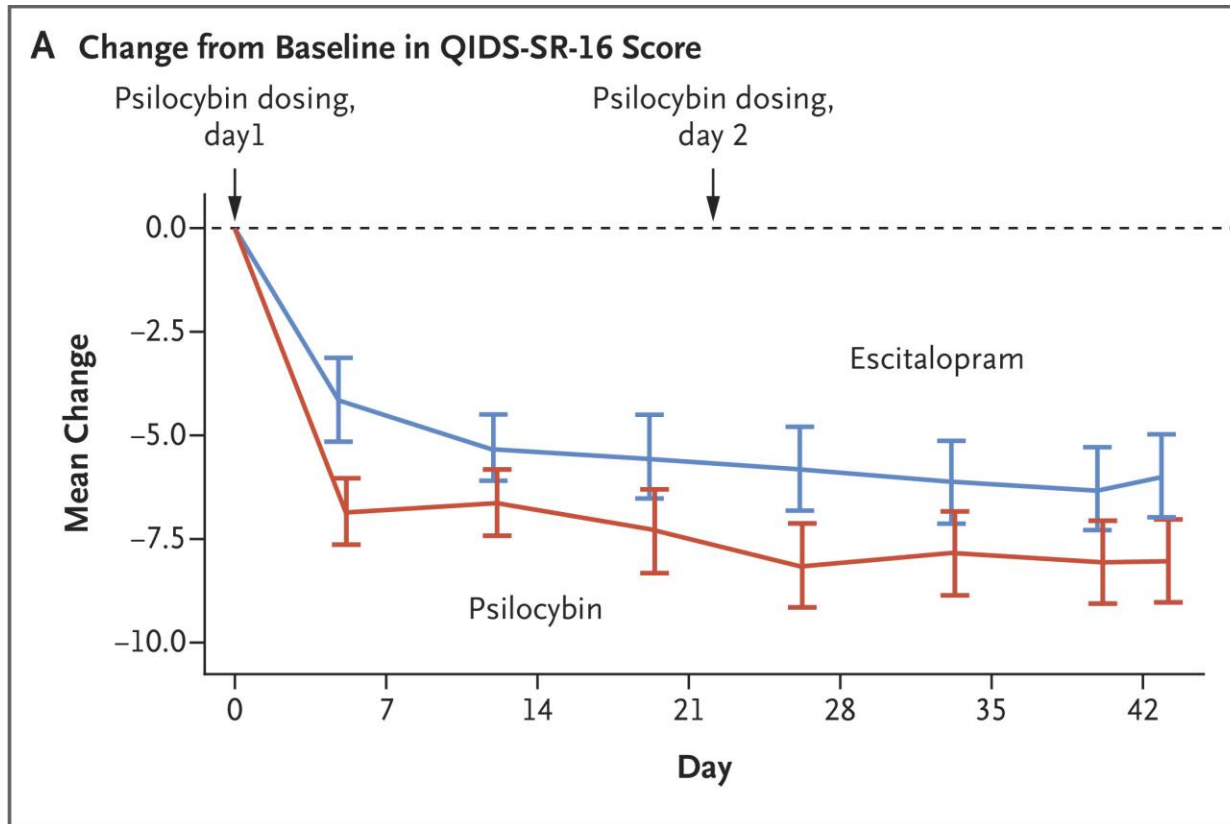
## Trial of Psilocybin versus Escitalopram for Depression

**Authors:** Robin Carhart-Harris, Ph.D., Bruna Giribaldi, B.Sc., Rosalind Watts, D.Clin.Psy., Michelle Baker-Jones, B.A., Ashleigh Murphy-Beiner, M.Sc., Roberta Murphy, M.D., Jonny Martell, M.D., Allan Blemings, M.Sc., David Erritzoe, M.D., and David J. Nutt, M.D. [Author Info & Affiliations](#)

Published April 14, 2021 | N Engl J Med 2021;384:1402-1411 | DOI: 10.1056/NEJMoa2032994 | **VOL. 384 NO. 15**

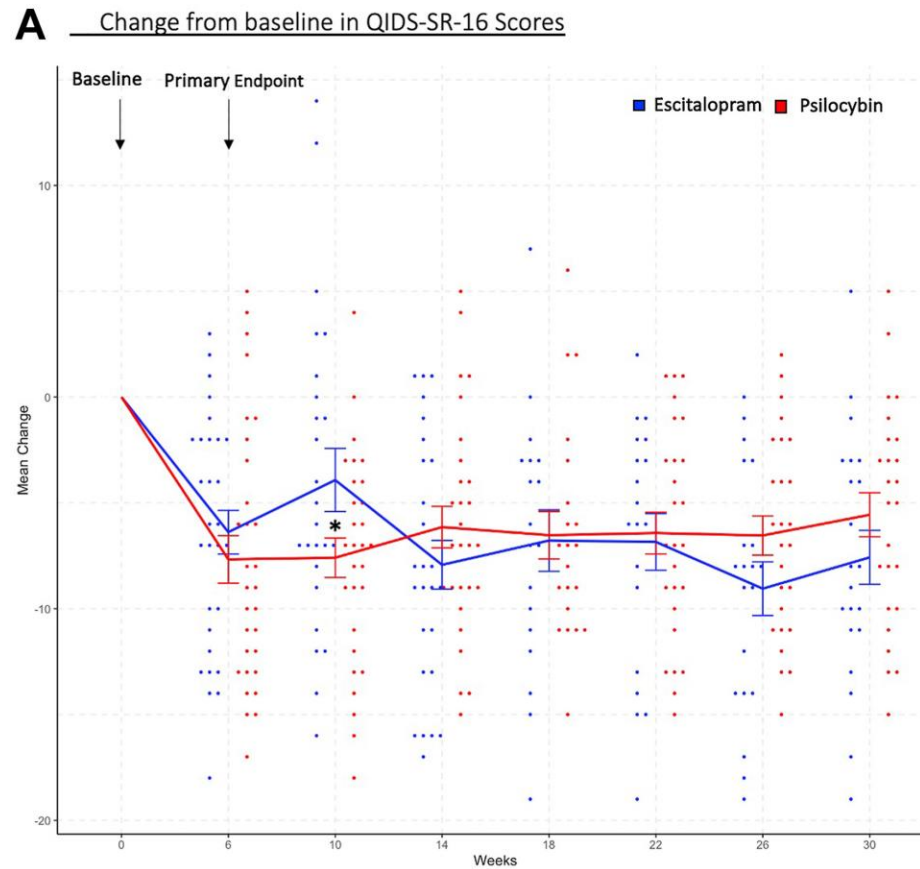
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# Psilocybin vs. Escitalopram





# Psilocybin vs. Escitalopram



Erritzoe et al., eClinical Medicine, 2024

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- What does “better” mean?
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- **How do we evaluate “better”?**
  - 2<sup>nd</sup> gen/depot antipsychotics: Comparative effectiveness
  - Xanomeline-Trospium: Cost-effectiveness
- How are we trying to get better?

# The CATIE Trial

## *The* NEW ENGLAND JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

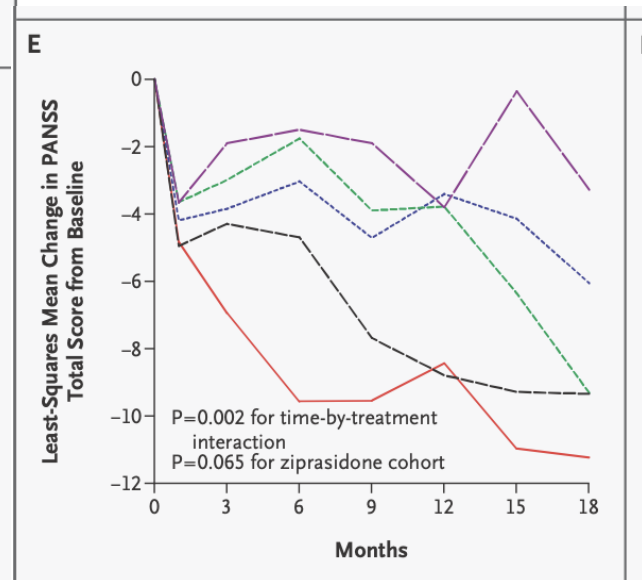
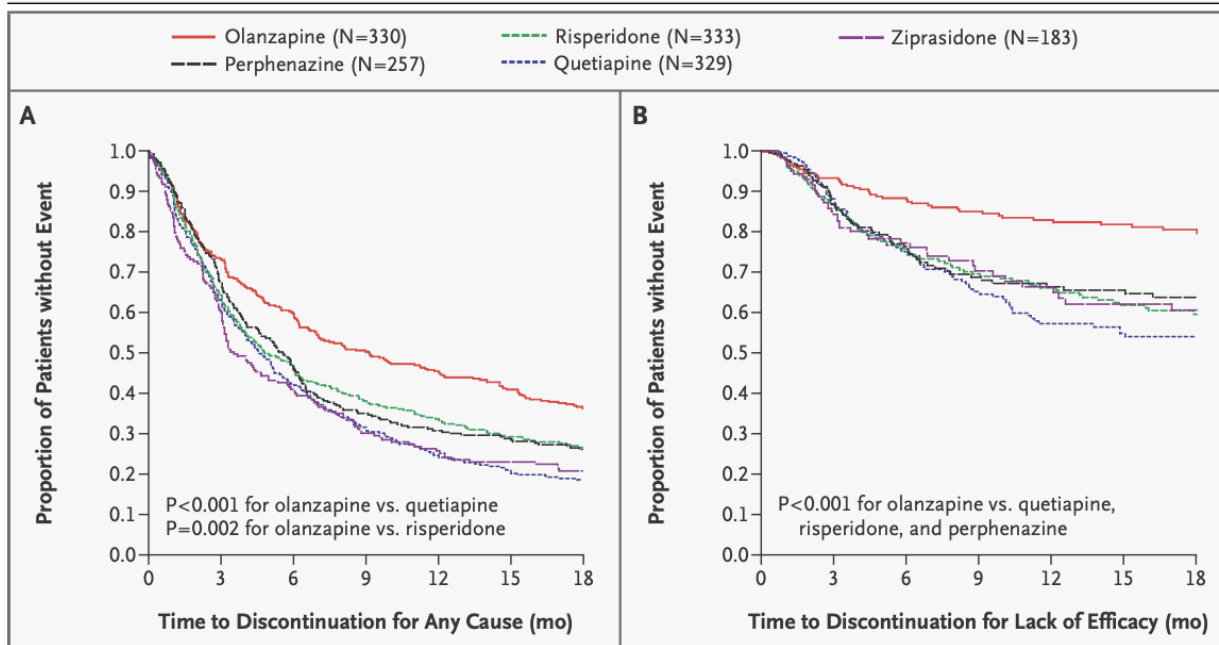
SEPTEMBER 22, 2005

VOL. 353 NO. 12

### Effectiveness of Antipsychotic Drugs in Patients with Chronic Schizophrenia

Jeffrey A. Lieberman, M.D., T. Scott Stroup, M.D., M.P.H., Joseph P. McEvoy, M.D., Marvin S. Swartz, M.D.,  
Robert A. Rosenheck, M.D., Diana O. Perkins, M.D., M.P.H., Richard S.E. Keefe, Ph.D.,  
Sonia M. Davis, Dr.P.H., Clarence E. Davis, Ph.D., Barry D. Lebowitz, Ph.D., Joanne Severe, M.S.,  
and John K. Hsiao, M.D., for the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) Investigators\*

# Conclusion: Olanzapine is Better Tolerated



# Long-acting Injectables



SUPPLEMENT ARTICLE | SEPTEMBER 30, 2016

## The Use of Long-Acting Injectable Antipsychotics in Schizophrenia: Evaluating the Evidence

Christoph U. Correll, MD (Chair); Leslie Citrome, MD, MPH; Peter M. Haddad, MD; John Lauriello, MD; Mark Olfson, MD, MPH; Stephen M. Calloway; John M. Kane, MD

J Clin Psychiatry 2016;77(suppl 3):1-24

# Long-acting Injectables

**Summary and conclusions.** LAIs are **superior to placebo** for acute and maintenance treatment of schizophrenia. Superiority of LAIs over oral antipsychotics is most pronounced in mirror-image studies that arguably are more representative of usual care patients and practices. In general, LAIs appear to be similar to one another in terms of relapse prevention, although differences in other domains have been reported.

**Summary and conclusions.** Nonadherence in patients with schizophrenia is common and difficult to detect. Although LAIs may provide one method to help improve treatment adherence, only a minority of medication nonadherent patients receive them. **Significant reductions in health care utilization or costs** associated with schizophrenia have been demonstrated in **some studies** of LAI antipsychotics, although other studies have not demonstrated these effects and showed cost-neutrality or even greater cost.

# Is Newer Better?



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VISUAL ABSTRACT



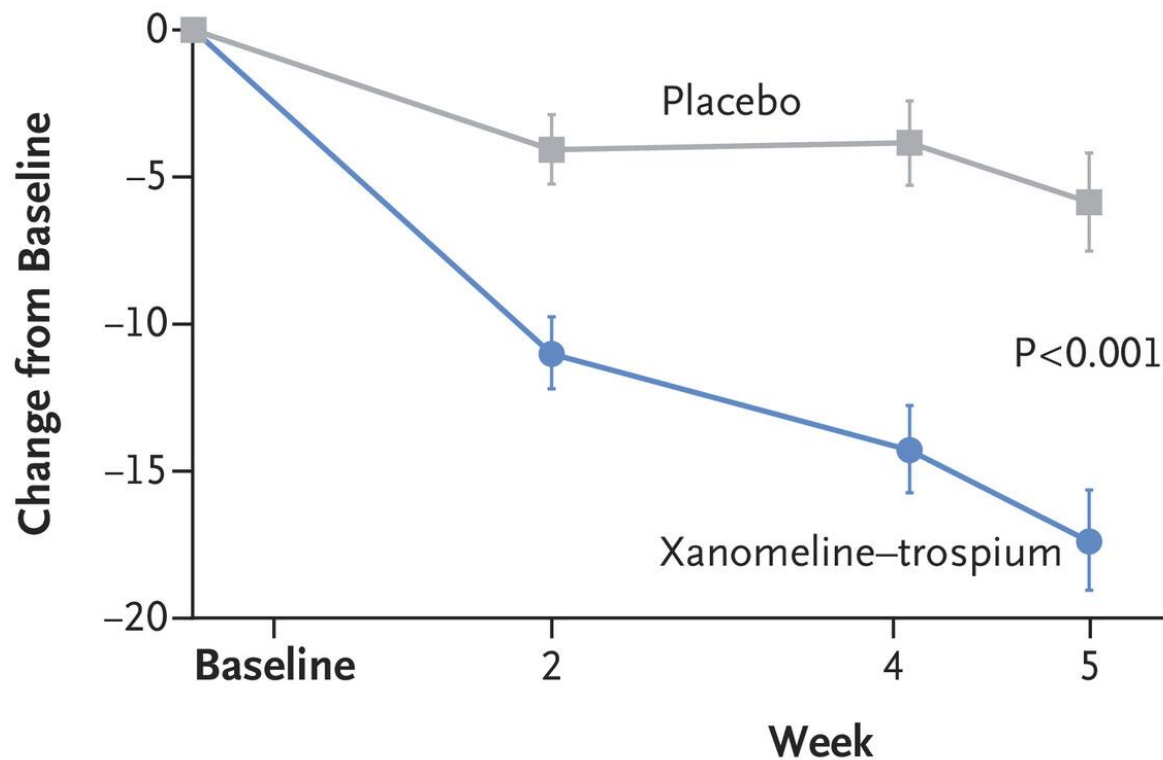
## Xanomeline–Trospium for Schizophrenia

February 24, 2021 | DOI: 10.1056/NEJMdo005976

SIGN IN  
TO S

# Is Newer Better?

## A PANSS Total Score





# Replication

## JAMA Psychiatry

### RCT: Efficacy and Safety of Xanomeline-Trospium in Schizophrenia

#### POPULATION

191 Males, 65 Females



Adults aged 18-65 y with schizophrenia experiencing acute psychosis

**Mean (SD), 43.1 (11.8) y**

#### SETTINGS / LOCATIONS



**30 Inpatient  
US/Ukraine  
sites**

#### INTERVENTION

256 Participants randomized



#### 125 Oral xanomeline-trospium

5-wk Treatment with xanomeline-trospium, titrated to 125 mg/30 mg twice a day



#### 131 Placebo

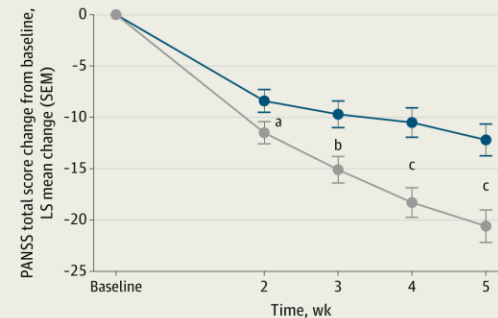
5-wk Treatment with placebo

#### PRIMARY OUTCOME

Change from baseline to week 5 in Positive and Negative Syndrome Scale (PANSS) total score with xanomeline-trospium vs placebo (range, 30-210 points; higher scores = greater symptom severity: 30, absent; 120, moderate; 210, extreme)

#### FINDINGS

Xanomeline-trospium significantly reduced PANSS total score from baseline to week 5 compared with placebo



**Least-squares (LS) mean (SE) change, -20.6 (1.6)**

**LS mean (SE) change, -12.2 (1.6)**

**LS mean difference, -8.4 (95% CI, -12.4 to -4.3;**

**P<.001; Cohen d, 0.60)**

Kaul I, Sawchak S, Walling DP, et al. Efficacy and safety of xanomeline-trospium in schizophrenia: a randomized clinical trial. *JAMA Psychiatry*. Published online May 1, 2024. doi:10.1001/jamapsychiatry.2024.0785

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# Cost-Effectiveness Analysis



## Schizophrenia

An assessment of xanomeline tartrate/trospium chloride (KarXT)

# Agenda

## Base-Case Results

Treatment with KarXT results in less time with diabetes and greater QALYs, greater life years, and greater evLYs. Using a placeholder annual cost of \$20,000 per year, the intervention costs are greater, but there are fewer non-intervention costs resulting from fewer relapses and treatment-emergent adverse events. Table 4.3 reports the base-case model outcomes for each arm of the model.

**Table 4.3. Results for the Base-Case**

Treatment	KarXT Cost	Total Cost	Years With Diabetes	QALYs	Life Years	evLYs
KarXT*	\$42,000	\$350,000	4.00	10.39	16.25	10.41
Aripiprazole	\$0	\$327,000	4.40	10.25	16.18	10.25

evLYs: equal-value life years, QALYs: quality-adjusted life years

\*Assuming a KarXT placeholder price of \$20,000 per year.

**Table 4.4. Incremental Cost-Effectiveness Ratios for the Base Case**

Treatment	Cost per QALY Gained	Cost per Life Year Gained	Cost per evLY Gained	Cost per Year Without Diabetes
KarXT*	\$163,000	\$347,000	\$146,000	\$60,000

evLY: equal-value life year, QALY: quality-adjusted life year

\*Assuming a KarXT placeholder price of \$20,000 per year.

# Cost-Effectiveness Analysis

## **Interventions of Interest:**

- Xanomeline tartrate/trospium chloride (Cobenfy, KarXT, Bristol Myers Squibb)

The independent appraisal committee voted that current evidence is not adequate to demonstrate superior net health benefits for KarXT compared to generically available aripiprazole.

If long-term data confirm KarXT's benefits and lack of weight gain, it would achieve common thresholds for cost-effectiveness if priced between \$16,000 to \$20,000 per year.

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  - Involvement of lived experience
  - Learning Healthcare

# AMP Schizophrenia


## Schizophrenia

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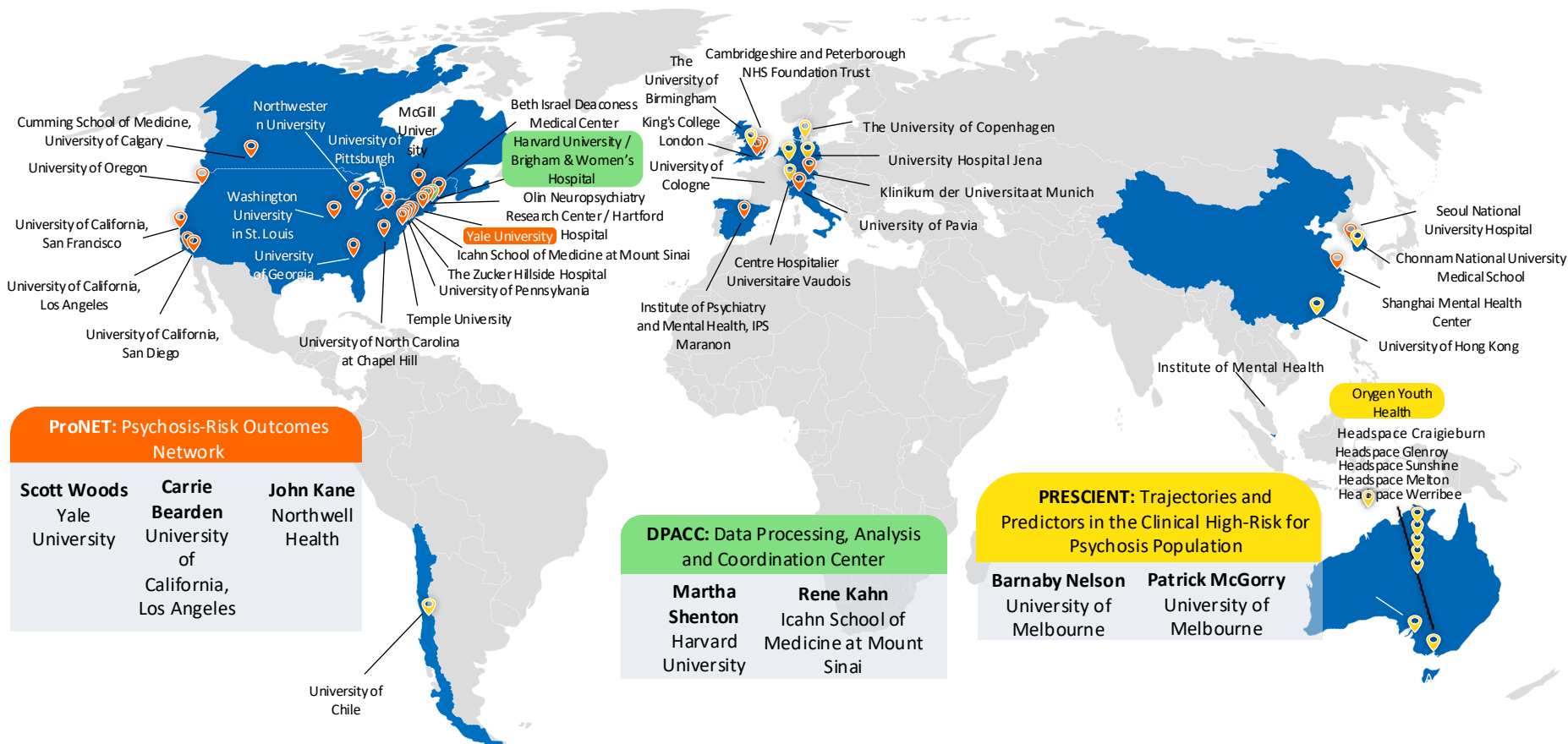
Editorial | [Open access](#) | Published: 15 April 2025

## Pathways to prevention: the Accelerating Medicines Partnership® Schizophrenia (AMP® SCZ) Program

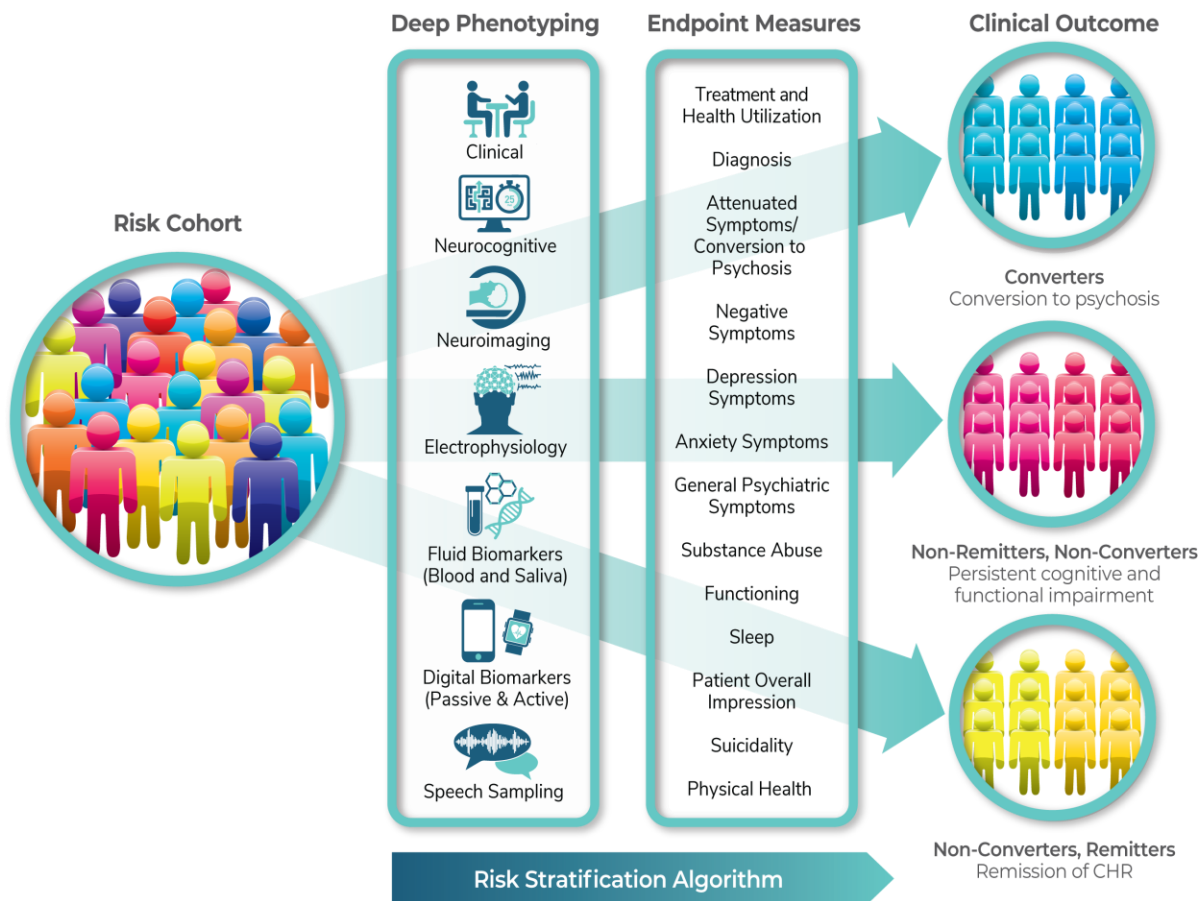
[Barnaby Nelson](#) , [Martha E. Shenton](#), [Scott W. Woods](#) & [the Accelerating Medicines Partnership® Schizophrenia \(AMP® SCZ\)](#).

[Schizophrenia](#) **11**, Article number: 62 (2025) | [Cite this article](#)

# A Global Research Network for Secondary Prevention in Psychosis



# Moving Earlier: AMP-Schizophrenia





# Integrating Lived Experience

## Schizophrenia

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### **Bridging Science and Hope: integrating and Communicating Lived experience in Accelerating Medicines Partnership® Schizophrenia Program**

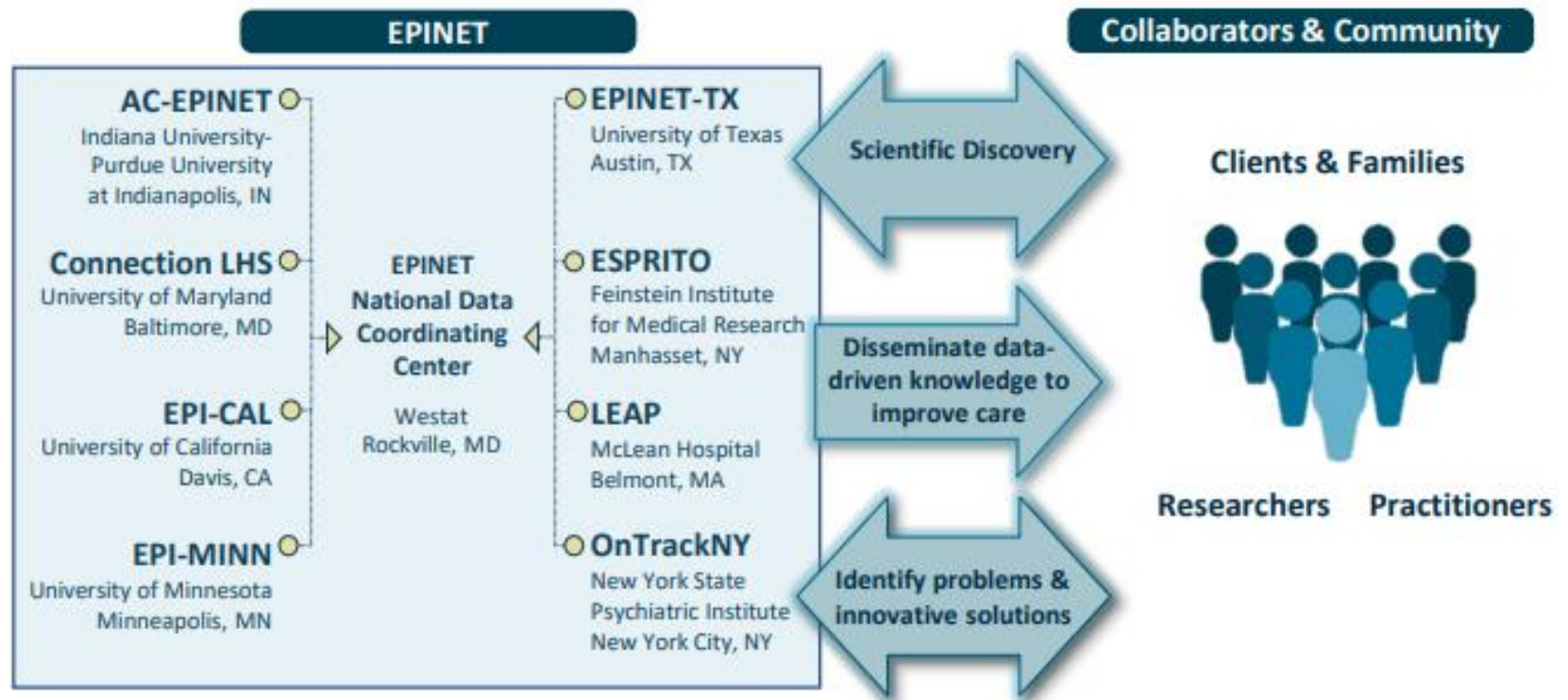
[Ameneh Asgari-Targhi](#), [Beier Yao](#), [Lisa Brown](#), [Suzanne Garcia](#), [Arundati Nagendra](#), [Kota Chin](#), [Tashrif Billah](#), [Nora Penzel](#), [Omar John](#), [Nicholas Prunier](#), [Simone Veale](#), [Elana Kotler](#), [Grace R. Jacobs](#), [Ming Zhan](#), [Michael J. Coleman](#), [Sylvain Bouix](#), [Ofer Pasternak](#), [Guillermo Cecci](#), [Justin T. Baker](#), [Daniel H. Mathalon](#), [Sinead M. Kelly](#), [Cheryl M. Corcoran](#), [Abraham Reichenberg](#), [Inge Winter-van Rossum](#), [the Accelerating Medicines Partnership® Schizophrenia \(AMP® SCZ\)](#), ... [Tina Kapur](#)  [+ Show authors](#)

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# Building a Learning Healthcare System for Early Psychosis



*Accelerating advances in early psychosis care, recovery outcomes, and scientific discovery through a national early psychosis learning health care partnership*



<https://www.cmhnetwork.org/news/nimh-launches-the-early-psychosis-intervention-network-epinet-a-national-learning-health-care-system/>

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