Avalere Health™

The use of patient-generated functional outcome measures in trials seeking to show improvements in negative symptoms or cognitive impairment associated with schizophrenia

Amrit Kaliasethi, MD MSc; Avalere Health, Knutsford, UK

Introduction and objectives

Poor real-world functioning, such as unemployment and dependent living, represents a significant burden in schizophrenia, primarily driven by negative and cognitive symptoms.[1,2] However, measuring real-world functioning poses challenges in pharmacotherapy trials aimed at improving these symptoms. Proxy measures of outcomes are categorized into activity-based and capacity-based measures.[3] Activity-based measures assess functioning through a patient's activities in key domains such as occupational and social, and can be reported by patients, carers, and clinicians. Capacity-based measures assess everyday functioning and can be determined by an interview-based assessment of the patient and their carer(s) by a clinician, or observing the completion of everyday activities or tasks in a controlled environment.

In schizophrenia treatment trials, activity-based measures using smartphones for patient-generated health data (PGHD) may address challenges in measuring real-world functioning. Two emerging smartphone-based innovations for PGHD include ecological momentary assessment or passive mobile sensing systems.[3] Despite the potential of these innovations, the level of adoption of smartphone-based PGHD measures in schizophrenia trials remains unclear.

Methods

A review was conducted of recent Phase 2 and 3 clinical trials (2013-2023) in schizophrenia. Trials were identified from ClinicalTrials.gov using the terms "schizophrenia" with "negative symptoms" or terms specific to key negative symptom assessment tools (PANNS, NSA-16, NSA-4, CGI-SCH scale, SANS, CAINS, BNSS); and "schizophrenia" with "cognition" or key cognitive assessment instruments (MATRICS, MCCB, BACS, CSB, CANTAB, RBANS, SCIP). Trials of the efficacy of pharmacotherapies for schizophrenia were included, whereas trials focused exclusively on assessing the safety, tolerability, or pharmacokinetics of pharmacotherapies, or those addressing all three aspects, were excluded.

Results

A total of 224 trials examining treatments for schizophrenia were identified. After deduplication, 106 unique trials were screened, and 67 fulfilled the inclusion criteria. Just under half of the trials (46.3%, 31/67) assessed the functional status in patients with schizophrenia. Of these trials, 58.1% (18/31) included at least one activity-based endpoint while 22.6% (7/31) included at least one functional capacity endpoint. Just under one-fifth (19.4%, 6/31) included both types of functional status endpoints (Figure 1). PGHD-based endpoints (a type of activity-based endpoint) derived from key emerging technologies were not included in any of the included trials. The most frequently used functioning status measurement tool was PSP (61.3%, 19/31), an interview-based, clinician-rated, activity-based measure (Figure 2). Overall, interview-based, clinician-rated measurement tools were the most common approach to evaluating functional status in patients with schizophrenia (67.8%, 21/31).

Figure 1: Proportion of pharmacotherapy trials (2013-2023) in schizophrenia by type of proxy measure of functioning included as an endpoint (N=31)

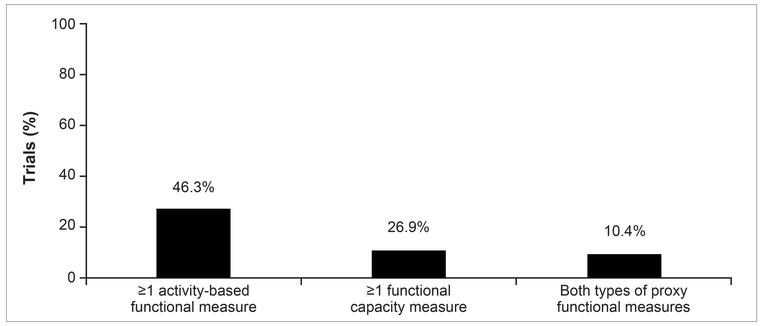


Figure 2: Proportion of pharmacotherapy trials (2013-2023) in schizophrenia that include a specific proxy measure of functioning as an endpoint (N=31)

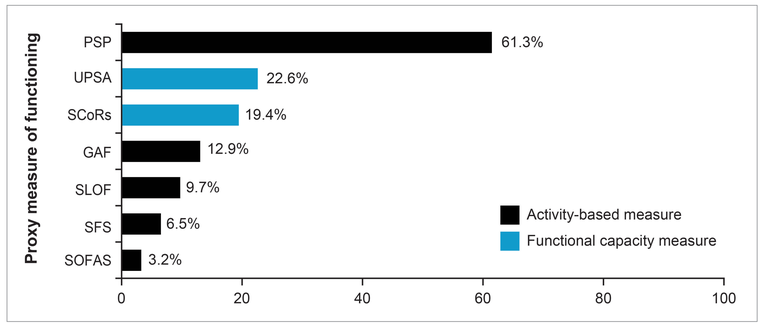
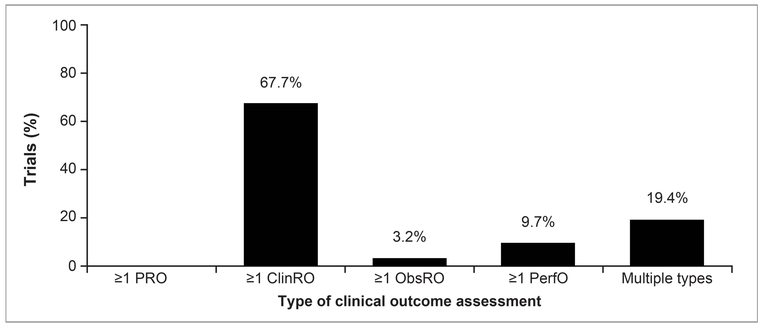


Figure 3: Proportion of pharmacotherapy trials (2013-2023) in schizophrenia including any proxy measure of functioning as an endpoint by type of clinical outcome assessment (N=31)



Conclusions

While there is a belief that smartphone-based PGHD measures are a feasible, reliable, valid, and cost-effective method to assess functioning in schizophrenia, this has not resulted in their inclusion in recent clinical trials for negative symptoms or cognitive impairment.

Currently, trials typically use traditional activity-based assessments which mainly rely on clinician ratings derived from structured interviews with patients who provide retrospective, self-reported data. However, the validity of self-reported data can be limited, particularly for patients with cognitive impairment.

The challenges associated with traditional measures, coupled with the value payers place on showing functional improvements when evaluating new treatments for schizophrenia,[4] drive the need for specific guidance on the development and use of smartphone-based PGHD measures for functional outcomes in regulatory and reimbursement decision-making.

References

1. Ventura, J. et al. (2009) 'Symptoms as mediators of the relationship between neurocognition and functional outcome in schizophrenia: a meta-analysis', Schizophrenia Research, 113(2–3), pp. 189–199. Available at: https://doi.org/10.1016/j.schres.2009.03.035.
2. McCutcheon, R.A., Keefe, R.S.E. and McGuire, P.K. (2023) 'Cognitive impairment in schizophrenia: aetiology, pathophysiology, and treatment', Molecular Psychiatry, 28(5), pp. 1902–1918. Available at: https://doi.org/10.1038/s41380-023-01949-9.
3. Searle, A. et al. (2022) 'Measuring functional outcomes in schizophrenia in an increasingly digital world', Schizophrenia Research. Cognition, 29, p. 100248. Available at: https://doi.org/10.1016/j.scog.2022.100248.
4. Kilburg, A. et al. (2014) 'Outcomes In Schizophrenia: What Does "Clinically Meaningful" Mean To Payers?', Value in Health, 17(3), p. A57. Available at: https://doi.org/10.1016/j.jval.2014.03.336.

Abbreviations

BACS, Brief Assessment of Cognition in Schizophrenia; BNSS, Brief Negative Symptom Scale; CAINS, Clinical Assessment Interview for Negative Symptoms; CANTAB, Cambridge Neuropsychological Test Automated Battery; CGI-SCH, Clinical Global Impressions-Schizophrenia; ClinRO, Clinician-Reported Outcome; COA, Clinical Outcome Assessment; CSB, CogState Schizophrenia Battery; GAF, Global Assessment of Functioning; MATRICS, Measurement and Treatment Research to Improve Cognition in Schizophrenia; MCCB, MATRICS Consensus Cognitive Battery; NSA-16, Negative Symptom Assessment-16; NSA-4, Negative Symptom Assessment-4; ObsRO, Observer-reported outcome; PANSS, Positive and Negative Syndrome Scale; PerfO, Performance Outcome; PRO, Patient-reported outcome; PSP, Personal and Social Performance; RBANS, Repeatable Battery for the Assessment of Neuropsychological Status; SANS, Scale for the Assessment of Negative Symptoms; SCIP, Screen for Cognitive Impairment in Psychiatry; SCoRs, Schizophrenia Cognition Rating Scale; SFS, Social Functioning Scale; SLOF, Specific Levels of Functioning; SOFAS, Social and Occupational Functioning Assessment Scale; UPSA, University of California San Diego Performance-Based Skills Assessment

Poster presented at ISPOR US, May 5–8, 2024, Atlanta, GA, USA