Valuation of Cognitive Impairment in Schizophrenia

Irene Santi[1], Andrew Lloyd[2], Claudia Hastedt[3], Matthijs Versteegh[1]

Background and objectives

- Loss of cognitive function is a common feature in schizophrenia and treatments are in development to address this. [1,2]
- Generic measures of health-related quality of life favoured by decision makers for cost-effectiveness analyses, such as the EQ-5D, are not designed to detect changes in cognitive function. [3,4]
- The disease-specific, interview-based Schizophrenia Cognition Rating Scale (SCoRS) is developed to measure the impact of cognitive impairment on everyday functioning. [5]
- The purpose of this study was to derive utilities based on this disease-specific instrument, for use in cost-effectiveness analysis.

Methods

- Key dimensions of cognitive impairment were selected from the SCoRS and valued by composite Time Trade-off (cTTO).
- A health state classification system was derived from the SCoRS based on the five most relevant items that accurately reflect the scoring performance of the SCoRS, selected by factor analysis, principal component analysis, item response theory analysis, correlation with cognitive performance using clinical trial data (N= 509, ClinicalTrials.gov, number NCT02832037) [6], and expert opinion. A limit to 5 items was necessary to reach a feasible level of complexity for the subsequent steps. The selected items are presented in Table 1.
- An orthogonal design was used to define an empirical set of health state vignettes. A total of 16 vignettes were randomly divided into two groups and assessed using interviewer-supervised cTTO. Members of the UK general population aged ≥ 18 years were recruited.
- Data were modeled using random effects (RE) and Tobit models. Model performance was evaluated based on goodness of fit. All estimated models used Level of Severity 1 ("None") as the reference category. Levels 2/3/4 represented mild/moderate/severe levels of impairment, respectively.
- Sensitivity to change of the developed scoring algorithm compared to EQ-5D was measured by correlation of the effect size (ES) and standardized response mean (SRM) using clinical trial data with complete 12-week MATRICs Consensus Cognitive Battery (MCCB) (N=445).

Results

- Five out of 20 SCoRS items were selected for the cTTO valuation study.
- A total of 400 participants from the UK were included in the final sample. Sample characteristics were similar to the UK general public.

Table 1. Selected SCoRS dimensions and corresponding items

Attention	Learning	Processing speed	Social cognition	Memory
Do you have difficulty…				
staying focused?	learning new things?	speaking as fast as you would like?	understanding what people mean when they are talking to you?	remembering information and/or instructions recently given to you?

- Both the RE and Tobit model reported insignificant results for level 2 and 3 (mild vs. moderate) of attention, for level 2 of processing speed and for level 2 of memory (none vs. mild). When combining level 2 and 3 (mild and moderate impairment) of attention, the corresponding coefficient was statistically significant in both models (Table 3).
- The mean cTTO value ranged from 0.152 for the health state "44444" to 0.855 for the state "41111".
- The utility scores derived from the SCoRS items by cTTO had higher and significant correlations with MCCB than EQ-5D when applied to clinical data (Table 2).

Table 2. Correlation of ES and SRM of MCCB, SCoRS_TTO and EQ-5D

	MCCB	
	Effect size (ES) Spearman's rho (p-value)	Standardized response mean (SRM) Spearman's rho (p-value)
EQ-5D	0.03 (0.552)	0.03 (0.535)
SCoRS_TTO	-0.22 (<.001)	-0.21 (<.001)

MCCB, MATRICs Consensus Cognitive Battery; SCoRS, Schizophrenia Cognition Rating Scale; SCoRS_TTO, cTTO valued SCoRS items

Table 3. Estimated disutilities –final RE model

Variables	Level*	β	SE	p-value
Attention	2 & 3	-0.019	0.009	0.036
Attention	4	-0.104	0.011	<0.0001
Learning	2	-0.041	0.013	0.002
Learning	3	-0.063	0.011	<0.0001
Learning	4	-0.180	0.011	<0.0001
Processing speed	2	-0.013	0.011	0.239
Processing speed	3	-0.064	0.013	<0.0001
Processing speed	4	-0.130	0.011	<0.0001
Social cognition	2	-0.046	0.013	<0.0001
Social cognition	3	-0.097	0.013	<0.0001
Social cognition	4	-0.236	0.011	<0.0001
Memory	2	-0.011	0.011	0.363
Memory	3	-0.055	0.011	<0.0001
Memory	4	-0.157	0.011	<0.0001
Constant		0.959	0.021	<0.0001

*Level of severity: 2, mild; 3, moderate; 4, severe.
RE, random effects.

Conclusions

- The results of this study show that it is possible to identify and value different levels of cognitive functioning separately.
- The developed scoring algorithm showed discriminative validity and sensitivity to change when applied to clinical trial data and can be used to derive health utility estimates to use alongside other outcomes data for health economic evaluation of treatments for cognitive impairment in patients with schizophrenia.

Affiliations
1 Institute for Medical Technology Assessment, Erasmus University Rotterdam, Rotterdam, The Netherlands
2 Acaster Lloyd Consulting Ltd, London, United Kingdom
3 Boehringer Ingelheim International GmbH, Ingelheim am Rhein, Germany

Disclosures
This project was funded by a research grant of Boehringer Ingelheim. The study was conducted independently and the researchers had contractually guaranteed freedom of publication.

References
1 Strassnig MT et al. Schizophr Res 2015; 165: 76–82.
2 Keefe RS et al.Biol Psychiatry 2005; 57: 688–91.
3 Krabbe, PFM et al. J Clin Epidemiol. 1999;52(4):293–301.
4 Geraerds AJ et al. Quality of Life Research. 2019 Jul;28(7):1931-9.
5 Keefe RS et al. American Journal of Psychiatry. 2006 Mar 1;163(3):426-32.
6 Fleischhacker WW et al. Lancet Psychiatry. 2021 Mar;8(3):191-201.