



Economic considerations of cognition and functional outcomes in patients with schizophrenia: A systematic literature review



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ABSTRACT

Background: The primary focus of research in schizophrenia has been on the positive symptoms, with findings that clearly establish their economic burden. More recently, research has expanded to focus on another core symptom of schizophrenia, namely cognitive impairments. While this work has established the adverse impact of cognitive impairments associated with schizophrenia (CIAS) on functional outcomes, their relationship to the economic impact of schizophrenia has not been systematically evaluated.

Objective: The aim of this research was to perform a systematic literature review identifying evidence that evaluates: 1) the economic impact of CIAS and its treatments, including health-state utilities, and 2) the economic evidence associated with improvements in the Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) Consensus Cognitive Battery and the University of California Performance Skills Assessment (UPSA).

Method: A systematic search of articles published from January 1999–April 2013 was conducted. Studies reporting direct costs, indirect costs, and quality of life impacts of CIAS and costs of CIAS interventions were reviewed.

Results: Forty-three studies met inclusion criteria. Twenty-four focused on indirect costs (work-related outcomes) associated with cognitive impairments and 14 studies included residential status outcomes. Four studies concentrated on the direct cost of cognitive remediation therapy. Three studies reported quality of life outcomes, but none used health-state utilities. Eight studies focused on the UPSA and its relationship to community outcomes. Only two studies were cost-effectiveness analyses.

Conclusions: Despite the growing scientific literature relating CIAS to adverse outcomes, the translation of outcomes into economic outcomes is seldom reported. Should novel pharmacotherapies and/or psychosocial treatments require reimbursement from health authorities and/or other payers, many gaps warrant attention in order to demonstrate the economic value of these therapies.

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1. Introduction

The current approaches to pharmacological treatment of patients with schizophrenia are based upon stabilization of psychotic symptoms through the use of antipsychotic therapies. The ability of first- and second-generation antipsychotics to stabilize patients and to reduce the incidence of costly relapse is well-documented. (Leucht et al., 2012) Moreover, the literature is replete with studies evaluating differential effectiveness and cost-effectiveness within the array of treatments administered to patients with schizophrenia for treatment of psychotic symptoms. (Ascher-Svanum et al., 2009; Edwards et al., 2005; Furiak et al., 2009; Heeg et al., 2005) However, two other core symptoms of schizophrenia also merit economic analysis, cognitive impairment and negative symptoms, because these symptoms may also

represent manifestations significantly associated with the cost of the illness. The focus of this paper is the body of literature documenting the economics of cognitive impairment associated with schizophrenia (CIAS) and its treatments.

Nearly every patient with schizophrenia experiences a cognitive decrement from the premorbid state. (Keefe, 2008; Keefe et al., 2005; Manschreck and Boshes, 2007) Even patients with neuropsychological test scores similar to healthy controls have comparatively lower mean functional performance scores. (Keefe et al., 2005; Kremen et al., 2000) There is an extensive literature documenting the aspects of function (e.g., social functioning, residential, occupational functioning, and quality of life) associated with CIAS. Studies of patients with other psychiatric disorders have documented differences in costs and economic burden in patients who do, versus who do not, have cognitive impairments (e.g., Mackin et al., 2011). Research in patients with schizophrenia has shown that those with higher functional and cognition scores predictably achieve significant employment and residential milestones, such as independent living

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status and employment status. (Harvey et al., 2009) The question of whether improving cognition results in economic benefits remains and has yet to be examined systematically, largely because of the lack of currently available effective treatments.

There is evidence supporting the clinical benefits of cognitive remediation therapy (CRT), in both conventional and computerized formats. (Patel et al., 2010; Wykes et al., 2007) However, these benefits were realized only when added to another form of psychiatric rehabilitation (e.g., supported employment, strategy training) versus adding CRT to usual care. (McGurk et al., 2007; Wykes et al., 2011) Cognitive remediation methods are still developing, and there remains uncertainty over which techniques should be employed and whether the outcomes are beneficial in terms of sustained effects on cognition or improved functioning. (National Institute for Health and Clinical Excellence, 2009) Due to variability in methodological rigor of the studies and the observed effectiveness of cognitive remediation, further research is required.

In addition to psychosocial treatments, pharmacotherapies have also been identified as potentially viable options for improving cognition. In recognition of the need to facilitate the study and registration of pharmacologic agents for the treatment of CIAS, the US National Institute of Mental Health (NIMH) developed an initiative called “Measurement and Treatment Research to Improve Cognition in Schizophrenia” (MATRICS). In partnership with the US Food and Drug Administration (FDA), industry, and academia, NIMH developed and published a consensus statement regarding how pharmacologic agents for the treatment of CIAS may be assessed (<http://www.matrics.ucla.edu/matrics-recommendations.shtml>). The MATRICS task force developed the MATRICS Consensus Cognitive Battery (MCCB) and selected it, along with a performance-based measure: the University of California Performance Skills Assessment (UPSA), as co-primary trial outcomes for evaluation of new therapies. Demonstrating benefit according to these measures is the first step in establishing the efficacy of novel pharmacotherapies to treat CIAS.

In addition to meeting efficacy hurdles, new therapies for CIAS will have to meet an array of economic expectations and demonstrate value for money in order for them to be reimbursed and made available to patients in need of treatment. The pursuit of economic evidence in parallel with efficacy assessments is critical due to decreases in the availability of health care funds. Understanding the current state of economic evidence regarding CIAS and its treatments is a prerequisite for establishing a foundation of knowledge from which to build future research. The aim of this study was to perform a systematic literature review to identify evidence evaluating: 1) the economic impact of CIAS and its treatments, including their impact on health-state utilities, and 2) the economic evidence associated with improvements in the Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) Consensus Cognitive Battery and the University of California Performance Skills Assessment (UPSA).

2. Methods

Systematic searches of English language articles published from January 1999 through April 2013 were conducted in multiple databases: PubMed, EMBASE, MEDLINE In-Process & other Non-Indexed Citations, EconLit, PsycINFO, and Clinicaltrials.gov. Abstracts from scientific conferences were also searched including: Schizophrenia International Research Society (SIRS), International Congress on Schizophrenia Research (ICOSR); American College of Neuropsychopharmacology (ACNP); European College of Neuropsychopharmacology (ECNP), Mt. Sinai Conference on Cognition in Schizophrenia, the European Conference on Schizophrenia Research, American Psychological Association, and the International Society of Pharmacoeconomics Research (ISPOR). Articles before 1999 were excluded because, before that time, there was limited

evidence regarding cognitive impairments, their functional consequences or appropriate interventions to address them. (Green, 1996; Bellack et al., 1999).

The literature search terms were developed to capture studies providing pharmacoeconomic information on direct and indirect costs, quality of life assessments associated with CIAS, as well as costs of CIAS treatments. Direct costs are defined as those incurred for medical treatment, such as visits with a physician, emergency room costs, hospitalization costs, community mental health costs, etc. Indirect costs are those associated with lost productivity/work due to patient disability, lost productivity/work by caregivers, societal costs (e.g., incarceration), etc. Literature regarding quality of life was included because of the importance of these measures in the calculation of the quality adjusted life year (QALY), which is widely used as the denominator of cost-effectiveness ratios in economic analyses. For several countries, this metric is a critical component of evaluations that determine reimbursement for new pharmaceutical therapies.

The literature included in this review was specific to that dealing with economic, societal, residential and occupational outcomes of patients with schizophrenia. The structure of the final search strategy for PubMed, including search terms and limits, is shown in Table 1 with references from search #6 being saved for review. This strategy was adapted for searches in the additional databases listed above. References from these searches were then reviewed using the inclusion and exclusion criteria detailed in Table 2.

Included studies were required to contain at least one reference to direct costs, indirect costs, costs associated with cognitive therapies or quality of life measurement. Reference lists of included studies were also reviewed for additional potentially relevant studies. Included studies were assessed for similarities with respect to study design, treatment examined (if any), and outcomes evaluated. Results of studies with similar outcomes/treatments were compared. Included studies were also assessed chronologically to determine how research in this area has evolved over time.

3. Results

Table 3 displays the characteristics of the 43 included studies. Twenty-four of these studies focused on work-related effects of cognitive deficits, such as wages earned, hours worked, employment status, and patient level predictors (PLPs) of employment (column 7 of Table 3). Four studies concentrated on cost-related outcomes of CRT. There were three studies reporting quality of life (QoL) outcomes, but none of these assessed QoL using health-state utilities. Nine of the included studies focused on the ability of UPSA to identify patients most likely to achieve improved functional milestones. Of the 43 studies, nine were randomized-controlled trials (RCTs), 32 had an

Table 1

PubMed search strategy (also customized for Embase, Medline In-Process, The Cochrane Library, and clinicaltrials.gov).

Search #	Term
1	(schizophrenia[MeSH]) AND (“cognitive deficit syndrome” OR cognition OR cognitive OR “cognitive impairment” OR neurocognition OR neurocognitive)
2	#1 limited to: editorial, letter, comment, case report
3	#1 NOT #2
4	#3 limited to: animals
5	#3 NOT #4
6	#5 AND (economic OR cost-effectiveness OR cost* OR burden OR productivity OR value OR societal OR financial OR resource OR absenteeism OR disability OR employment OR vocational OR occupational OR expenditure OR “quality-adjusted life years” OR residential)

* truncated term.

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