Targeted Literature Review (TLR) of the Economic Burden of Cognitive Impairment Associated With Schizophrenia (CIAS)

PMH42

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Introduction

- The prevalence of schizophrenia worldwide is estimated at 1% (Leucht 2007) and the 5th leading cause of years lost due to disability among men (WHO 2004).
- Cognitive deficits in schizophrenia are often overlooked and are generally not responsive to existing therapies. These deficits have a profound impact on activities of daily living and quality of life (Sevy 1995).
- The economic impact of schizophrenia is significant, with an estimated total cost of $62.7 billion attributed to the condition in the United States (US) in 2002 (Wu 2005).
- Although the costs associated with schizophrenia are well documented, the costs arising from cognitive impairment are not well studied, which makes estimating the economic impact of these symptoms uncertain.

Objective

- The targeted literature review for the economic burden of disease searched for published data quantifying the direct and indirect costs associated with CIAS, and data describing resource use patterns and trends in this patient population. Accordingly, a targeted literature review was performed to:
  1. Identify the current economic burden of CIAS, including:
     - Direct healthcare costs (e.g., costs associated with hospitalizations)
     - Indirect healthcare costs (e.g., disability, days missed from work, caregiver burden)
     - Healthcare resource use (e.g., number of inpatient and outpatient hospitalizations)
  2. Identify evidence gaps

Methods

Literature Search

- Searches were performed in MEDLINE with MEDLINE® E-pubs ahead of print, Embase, EconLit (Ovid SP®), NHS Economic Evaluations Database (NHS EED), and the Cochrane HTA Database guide.
- The search strategy originally targeted literature with a clearly defined focus on CIAS patients; however, due to the lack of available studies, general schizophrenia studies were included if they contained economic data of interest such as direct costs, indirect costs, and healthcare resource utilization (HCRU).
- Conference proceedings for the last 2 years were searched for the International College of Neuropsychopharmacology (CINP) World Congress, Society for Research in Psychopathology, European Conference on Schizophrenia Research, and American College of Neuropsychopharmacology.

Study Selection

- One systematic reviewer screened abstracts and full texts according to the eligibility criteria outlined in **Table 1**.
- Preference was given to the most recent and robust studies, as assessed by independent reviewer, that met the eligibility criteria
- Publications were excluded based on the following:
  - Patient population (i.e., not CIAS, or general schizophrenia population)
  - For the general schizophrenia population, a geographic restriction was applied for the following regions: North America (United States and Canada); Europe; Asia (Japan and Hong Kong)
  - Study design (i.e., reviews, case studies, in vitro studies, erratum)
  - Outcomes not of interest (i.e., economic data pertaining to a specific intervention, HRQoL outcomes)
  - Duplicate records
  - Publication not in English

Table 1. Eligibility criteria for the economic burden targeted literature review

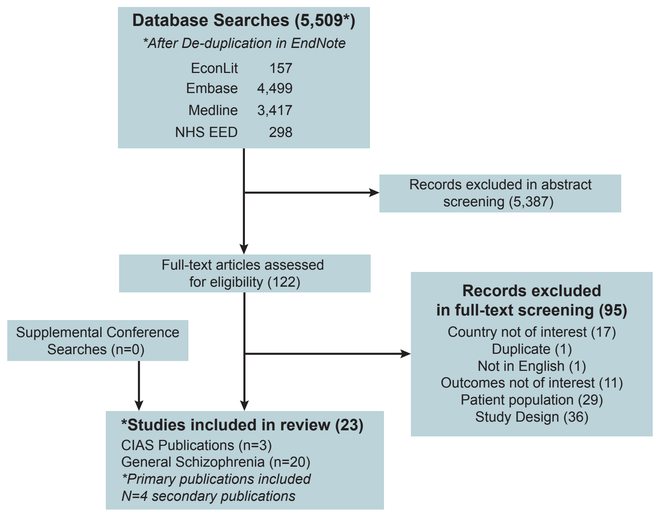
Category	Economic burden
Patients	Adult patients (≥18 years) with CIAS
Outcomes	Direct/indirect costs, resource use, and cost utility studies
Study design	Economic studies on the cost of disease (direct and indirect) and resource utilization
Geography	No restriction (for CIAS studies)
Limitations	• Only articles published in English were included • Only economic evidence published in the last 10 years (2007 to December 2017) was considered • Reviews and case reports were excluded

CIAS, cognitive impairment associated with schizophrenia.

Results

- A total of 27 articles, consisting of 23 primary studies and four secondary publications, were included in this economic literature review **(Figure 1)**

Figure 1. Flow chart of study selection



Results (continued)

- Fourteen publications were identified that provided information about healthcare resource utilization, and 13 that reported direct and indirect healthcare costs.
- The majority of these studies were conducted in a single country of interest, including: United States (US) (n=14), United Kingdom (UK) (n=2), Germany (n=1), France (n=1), Italy (n=2), Spain (n=1), Canada (n=1), Japan (n=1), and Hong Kong (n=1). Three studies were multinational or international (n=3).
- The most common patient population evaluated was the general schizophrenia population; however, five studies (three primary and two secondary) were identified pertaining to a CIAS-specific population.

CIAS Studies Economic Burden

Healthcare Resource Use, CIAS (n=5)

United Kingdom

- A majority of the information relating to resource use in a CIAS patient population came from a clinical trial of cognitive remediation therapy (CRT) and the subsequent cost-effectiveness analyses (Patel 2010, Reeder 2014, Wykes 2007).
  - Length of stay for hospitalizations or specialist accommodation was high, ranging from a mean of 21 days for specialist accommodation over a 3-month period (n=39 patients) (Patel 2010), to a mean of 59 days in 6 patients who were admitted to an acute psychiatric ward (Reeder 2014).
  - 19% of patients (16/84) reported at least one psychiatric outpatient visit in the prior 6 months, with a mean of 4.5 visits for this group; a further 7.2% reported other hospital outpatient visits (mean 1.3 visits) (Reeder 2014).
- Day center and counselling services were also used broadly; mean day center use during 6 months of follow-up was 18.4 days (Patel 2010).
- CIAS patients who attended group therapy in a 6-month period (7/83, 8.4%) reported a mean of 14.3 attendances (Reeder 2014).

United States

- Patients with lower community functioning (LCF) had fewer prior hospitalizations than those with higher community functioning (HCF) (7.4 and 8.3 for LCF vs. 9.6 and 9.3 for HCF) (Bell 2008).

Canada

- The crude hospitalization rate for schizophrenic disorders among people with an intellectual disability was 6.24 per person-year over a 5 year period, a ~15 fold increase compared to those without an intellectual disability (Balogh 2010).

Direct Healthcare Costs, CIAS (n=4)

- A majority of the direct healthcare cost results were summarised from one primary publication from the UK, and the associated secondary publications (costs were reported in 2000/2001 prices) (Patel 2010, Reeder 2014, Wykes 2007).
  - Total direct health and social care costs per patient ranged from £8,271 at 14 weeks of follow up to £13,426 at 40 weeks of follow up for the 'usual care' cohort (Wykes 2007).
  - Mean medication costs for antipsychotic medications during the 6 months prior to randomization were £890.63 (SD £654.85) (Reeder 2014).
  - Mean outpatient costs on the same basis were £269.40 (SD £763.37) in the 6 months before randomization (Reeder 2014).
  - Mean cost of special accommodation on the same basis was £6,387.01 (SD £11,072.49) in the 6 months before randomization (Reeder 2014).
- In the US, total mental healthcare costs per patient were $10,665 over 6 months and $56,394 over 24 months among older (≥60 years) cognitively impaired individuals with severe psychiatric conditions in the US (reporting year 2011) (MacKin 2011) **(Figure 2)**.

Figure 2. Total costs of mental health treatment in cognitively impaired vs cognitively intact patients with severe psychiatric disease

Source: Mackin 2011
USD, US dollar.

Indirect Costs, CIAS (n=3)

- No publications were identified that evaluated the caregiver burden of CIAS.
- Indirect costs were reported by one primary and two secondary studies that evaluated the cost-effectiveness of cognitive remediation therapy (CRT) vs. usual care (UC) in the UK (Patel 2010, Wykes 2007, Reeder 2014).
  - The average cost of social security benefits in the 6 months prior to randomization was £2,243.43 (SD £1,228.24, n=84) per patient (2000/2001 costs) (Reeder 2014).
  - Only 10% of trial participants were in paid or voluntary employment.[6]
  - In terms of societal costs, CRT was found to be cost saving by £1,284 during the treatment period (14 weeks) after adjustment for baseline variables; however, during the follow-up period (40 weeks), it was found to be more costly by £494 (Wykes 2007). These results should be interpreted with caution as the follow-up publications both found CRT to be cost saving from a societal perspective at both time points (14 weeks and 40 weeks post treatment) (Patel 2010, Reeder 2014).

Schizophrenia Studies Economic Burden

Healthcare Resource Use

- In the US, inpatient admissions ranged from a mean of 0.11 per patient per year for schizophrenia-specific hospitalizations, to 0.68 per patient per year for all-cause hospitalizations (Offord 2013).
  - All-cause hospitalization length of stay was lower at 2.8 days in a medication adherent group compared to 7 days in a low adherence group. Psychiatric hospitalizations followed the same pattern ranging from 0.7 days to 3.2 days in the respective adherent and non-adherent cohorts (Offord 2013).
- A German study found that the excess number of admissions attributable to schizophrenia was 0.89 per patient per year with an average length of stay of 25.56 days compared to the control population (Frey 2014).
- A Spanish study revealed a statistically significant higher mean number of outpatient visits were reported by a cohort of schizophrenic patients with negative symptoms compared to those without (Sicras-Mainer 2014).

Results (continued)

Total Direct Healthcare Costs

- In the US, the total direct healthcare costs of schizophrenia ranged from $7,577 per patient in a homeless cohort from 1998–2000 (Gilmer 2003) to $23,455 in a Medicaid cohort in 2013 (Cloutier 2016).
- In Europe, the total direct cost of healthcare ranged from €1,626.9019 per patient in Spain among schizophrenic patients without negative symptoms (consisting of general care and specialized care) (Sicras-Mainer 2014) to €20,609 per patient per year for patients with schizophrenia in Germany from a societal perspective (consisting of inpatient and outpatient visits, pharmaceutical costs, rehabilitation, and nursing services) (Frey 2014).

Medication Costs

- The cost of medications in the US range from $1,085 per patient per year for antipsychotic medications in a non-adherent medication cohort with Medicare insurance (Offord 2013) to an excess annual medication cost for schizophrenia of $3,500 in a commercially insured cohort (Cloutier 2016).
- Medication costs in Europe (in US dollars) over a 6-month period, adjusted by age, sex, and previous hospitalizations, ranged from $596 in the UK for healthcare users to $717 in Germany for non-healthcare users (Heider 2009).

Inpatient Costs

- Inpatient hospital costs accounted for approximately half of the economic burden for schizophrenia:
  - In the US, annual inpatient costs for psychiatric-related hospitalizations ranged from $10,111 in a commercially insured cohort to $13,965 for a Medicaid cohort (Lang 2013); an excess cost due to schizophrenia of $6,032 per patient per year was reported in a Medicare cohort, accounting for 49% of the total excess cost attributable to schizophrenia (Cloutier 2016).
  - In Germany, the excess inpatient costs due to schizophrenia were €5,610 per patient-year accounting for 50% of the total excess direct healthcare schizophrenia (Cloutier 2016).

Outpatient Costs

- In the US, outpatient mental healthcare costs range from $1,760 per patient per year in a homeless cohort to $3,873 per patient per year in a board and care cohort (Gilmer 2003).
- In Europe, day clinic costs for a 6-month period ranged from $66.00 per patient in the UK among non-healthcare users to $8,204 in France among healthcare users (Heider 2009).

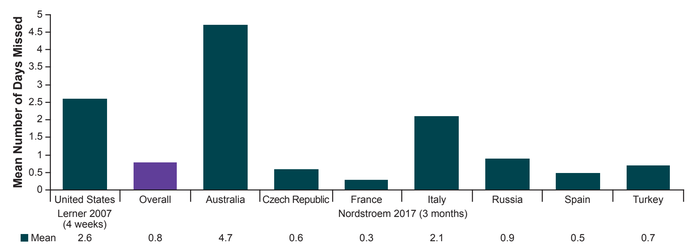
Institutionalization Costs

- Institutionalization costs were reported as €1,783.56 per patient per year in Italy (cost of nursing home care) (Esposti 2014).

Indirect Costs

- The excess indirect costs of schizophrenia in the US accounted for 76% of the overall economic burden (Cloutier 2016).
  - Unemployment accounted for 38% and $59 billion USD
  - Caregiving accounted for 34% and $52.5 billion USD
- In France, the annual indirect cost linked to unemployment was €2.214 billion (Sarlon 2012).
- Caregiver burden associated with schizophrenia led to an average of 0.8 days of missed work over a 3-month period in an international study (Australia, Czech Republic, France, Italy, Russian Federation, Spain, and Turkey) (Nordstroem 2017) to 2.6 days over a 4-month period (Lerner 2017) **(Figure 3)**.

Figure 3. Mean number of work days missed due to caregiving



Source: Nordstroem 2017, Lerner 2008

Knowledge Gaps

- Few studies assessing resource utilization, direct and indirect costs attributable to CIAS in all countries.
- The patient population for CIAS is not consistently defined. Despite the availability of multiple tools to assess cognition, there is no standard format for physicians to use in order to examine cognition in schizophrenia patients in the inpatient and outpatient settings.
- Schizophrenia is a frequently evaluated patient population in the literature of which CIAS is a subgroup. Although there are many estimates available, there is no evidence or publications that demonstrate the exact proportion of schizophrenia patients that have cognitive impairment.
- There is a clear lack of quantitative data detailing the economic impacts on caregivers of patients with CIAS. As a result of decreased cognition, these patients will likely require more one on one time with counsellors and more direct care from either a family member or legal guardian. Quantifying this will be important for future studies.
- Large database studies investigating a CIAS population are needed to quantify both HCRU and direct and indirect costs.

Conclusion

- The direct costs associated with treating CIAS are significant in the US and UK.
- There is a scarcity of data related to the economic burden incurred by patients with CIAS.
  - This review identified two additional HCRU publications and one direct cost publication that were not identified in a previous systematic literature review, adding to the evidence reported in this specific patient population.
- There is no evidence estimating the proportion of patients with schizophrenia that have cognitive impairment and how these symptoms affect the costs for treating schizophrenia.
- While there is significant literature on cognition as a strong predictor of functional outcomes, this has not been sufficiently studied to determine the relative impact on the economic burden of disease.

Disclosures

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