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Review

Direct healthcare cost of schizophrenia – European overview

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ABSTRACT

Purpose: To provide an overview on the magnitude of the impact of schizophrenia on the healthcare system in Europe and to gain a better understanding on the most important factors influencing the variation of costs.
Methods: Studies reporting costs and healthcare utilization among patients with schizophrenia were searched in MEDLINE (via Scopus), EMBASE (via Scopus) and Cochrane Database of Systematic Reviews on 19th January 2017.
Results: Twenty-three studies, from the 1075 references initially identified, were included in this review. The annual cost per patient ranged from €533 in Ukraine to €13,704 in the Netherlands. Notably drug costs contributed to less than 25% of the direct healthcare cost per patient in every country, which might be explained by similar pharmaceutical prices among countries due to the reference pricing system applied in Europe. Inpatient costs were the largest component of health service costs in the majority of the countries. Despite methodological heterogeneity across studies, four major themes could be identified (age, severity of symptoms, continuation of treatment/persistence, hospitalization) that have substantial impact on the costs of schizophrenia.
Conclusions: Schizophrenia represents a substantial cost for the healthcare system in Europe driven by the high cost per patient. Substantial savings could potentially be achieved by increasing investment in the following areas: (1) reducing the number of hospitalizations e.g. by increasing the efficiency of outpatient care; (2) working out interventions targeted at specific symptoms; (3) improving patient persistence and adherence in antipsychotic therapy.

1. Introduction

Schizophrenia represents one of the leading public health issues in psychiatry. The median (10–90 percentile) of point prevalence of schizophrenia was found to be 460 (190–1000), and the incidence was found to be about 15.0 (7.7–43.0)/100,000 in a systematic review that included studies from several regions of the World [1]. A comprehensive study including data from member states of the European Union (EU-27) plus Switzerland, Iceland and Norway [2] estimated that the prevalence of psychotic disorders is 1.2% in the EU population, and the estimated number of persons affected in 2011 was 5 million.

Existing antipsychotics can achieve full remission only in about 30% of schizophrenia patients and about 20–30% are resistant [3] showing a significant unmet need. Antipsychotics cause typical adverse effects (e.g. extrapyramidal symptoms, altered glucose metabolism) especially when administered in combinations [4]. Both the high rate of resistance and the need for adverse effect treatment result in an additional burden on health systems.

Individuals with schizophrenia use a substantial amount of healthcare services. This condition imposes a significant economic burden on both the patients and their families, and on society as a whole [5]. The interpretation of the cost-of-illness studies for schizophrenia can be difficult, due to the diversity in study design, reporting and the change in prices. The most recent systematic literature review, published in 2017, gives a comprehensive overview on the global economic burden of schizophrenia [6] from a societal perspective. The study shows high differences in

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the total societal cost across the globe varying from $US5818 in Thailand to $US 94,587 in Norway. We believe that a more detailed overview of the direct healthcare costs among schizophrenia patients in Europe might provide additional insight into the cost drivers and the factors explaining the variation of treatment costs across patient groups within a given country. This information can highlight certain aspects of the disease and processes of care where improvements are needed, and thus inform those involved in the planning of healthcare services and prioritizing research.

The development of systems of mental healthcare in Western Europe is characterized by a common trend toward deinstitutionalization, less inpatient treatment and improvement of community services [7]. The structure and capacity planning of inpatient care has been changed dynamically in recent years, leading to the strengthening of outpatient care provisions which reduce hospital bed days. The development of health care provision in the Central- and Eastern European (CEE) countries shows more inconsistencies. Recently, mental health policy began to change, new mental health legislation focusing on human rights was taken into effect and a deinstitutionalization process took place. However, in some CEE countries decrease in the number of psychiatric beds was not accompanied by adequate development of outpatient care and so it is often limited to drug prescription [8,9]. Consequently, in some countries recent trends in pharmaceutical therapies may have more influence on the direct costs of schizophrenia.

Our review included relatively recent papers published from 2010. Our aim was to balance between the requirements of HTA agencies preferring up-to-date data and to have sufficient information to draw conclusion. When initial date for inclusion was selected we considered that major policy and treatment changes with potentially significant impact on direct health care cost, including deinstitutionalization of patients, shift toward generic and/or long acting injectable drugs were implemented earlier than 2010. Hence the period since 2010 could reasonable be considered fairly homogenous period in the management of schizophrenia.

The objective of this overview was to provide an overview on the magnitude of the impact of schizophrenia on the healthcare system in Europe and to gain a better understanding on the most important factors influencing the variation of costs. More, specifically the review aims to address the following questions:

- What is the total direct healthcare cost per patient with schizophrenia in European countries?
- What is the relationship between European countries' economic wealth (GDP per capita) and direct healthcare cost per patient with schizophrenia?
- What are the most important factors associated with the variations in cost of schizophrenia across patient groups?

2. Methods

2.1. Databases and literature search strategy

The systematic literature search was conducted and reported in compliance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement [10], an external quality control benchmark. The literature search was performed in 19th January 2017 using MEDLINE (via Scopus), EMBASE (via Scopus) and Cochrane Database of Systematic Reviews.

The search strategy was built up as a combination of search strings related to the economic burden of schizophrenia. The detailed search strategy with number of hits can be found in Appendix A. The literature search was limited to English language papers published between 2011 and 2017. Due to the overlap of coverage between the databases, search results were de-duplicated first, followed by a title and abstract-based screening conducted by two independent reviewers (T.A., G.K). Disagreements were resolved by a third, principal researcher (A.T.Z.).

Studies were included if the *population* of interest had a clinical diagnosis of schizophrenia at any age and the study contained any cost or resource use data related to the treatment of schizophrenia. No restrictions on study *interventions*, *comparators* and study *outcomes* were used during the systematic literature review. Search results were considered in two steps. Initially, titles and abstracts of all articles were screened using the following exclusion criteria: (1) article is without abstract; (2) article is not English language paper; (3) article is editorial, letter or review; (4) article is case study/case series or the total sample number is $<$100; (5) article does not report data relevant to the research topic. Due to the potential limitations of electronic search strategies, reference lists of the excluded reviews were also checked for additional relevant studies. Articles deemed relevant were checked for eligibility in full-text. Publications were excluded if met any of the following criteria (1) in language other than English; (2) conference abstract or study protocol; (3) no European focus; (4) no relevant data; (5) data collection closed before the end of 2005 (i.e. if a study did not present any cost or resource use related from the period after December 31, 2005); (6) the number of the included persons $<$ 100; (7) review article; (8) data referred from other included articles.

2.2. Data extraction

A standardized data extraction form was developed and then checked for suitability. The following information was extracted from each included study: (1) the first author and year of publication; (2) the study perspective (i.e., societal, healthcare, third party payer or patient as sub-perspectives); (3) epidemiological approach (i.e., prevalence or incidence based); (4) study design (i.e., prospective or retrospective); (5) the country; (6) the cost calculation method: bottom-up (assessing the individual cost of persons with schizophrenia) or top-down (using national or regional statistics to withdraw the cost of the disease); (7) the year of analysis, pricing year and currency; (8) the diagnostic criteria for schizophrenia; (9) the characteristics of the study sample; (10) data on healthcare utilization (i.e., resource use data on inpatient care); and (11) data on direct healthcare costs (i.e., the resource consumption in the healthcare sector associated with the provision of healthcare interventions: e.g. the cost of hospital stays, outpatient visits and drugs). Costs and resource use estimates were extracted with regards to the related follow-up period, unit, and currency.

Data was retrieved per study arm from included studies that had a comparative design investigating differences in the cost of treatment across study groups. Based on these subgroup analyses we identified important factors and cost drivers that explain the variation of treatment costs across patient groups with schizophrenia.

2.3. Reporting cost estimates

To compare costs across studies, the costs were extrapolated to calculate annual costs per patient where necessary. Cost data reported in US dollars were converted into euro (€) using the average US dollar/euro exchange rate reported by the European Central Bank (https://www.ecb.europa.eu/stats/policy_and_exchange_rates/key_ecb_interest_rates/html/index.en.html) for the year of costing. Cost estimates were reported in two ways, reflecting the different purpose of our analyses: (1) The direct healthcare cost of