

## PHARMACOECONOMIC ASPECTS OF SCHIZOPHRENIA

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## ФАРМАКОЕКОНОМСКИ АСПЕКТИ СХИЗОФРЕНИЈЕ

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### ABSTRACT

Schizophrenia is one of the most serious psychiatric illnesses belonging to the group of non-affective psychoses. It is characterized by distortions of thought, perception, emotions and behavior. Twenty-four million people around the world suffer from schizophrenia. Schizophrenia is a chronic illness connected to significant expenses which are imposed on both the health system, extended social community and family, as well. Cost of illness studies of schizophrenia conducted around the world show wide range of material resources that countries set aside from their health budgets in order to cure schizophrenia. They range from 1.6% to 2.5%. International cost of illness studies came to the conclusion that the costs of this disease are high, depending on the health system and location and that intangible costs per se already justify investments in research and development of new treatments. Majority of published papers suggest that atypical antipsychotics have better cost-effectiveness profile in comparison to the first generation of antipsychotics. Olanzapine, clozapine and risperidone are atypical antipsychotics generally found to be most cost-effective in treating schizophrenia.

**Key words:** schizophrenia, pharmacoeconomics, cost of illness

### САЖЕТАК

Шизофренија је једна од најтежих психијатријских болести и спада у групу неафективних психоза. Карактерише се поремећајима мишљења, перцепције, емоција и понашања. Двадесет четири милиона људи широм света болује од шизофреније. Шизофренија је хронична болест повезана са значајним трошковима које осим здравственог система, сnose шира друштвена заједница и породица. Студије о трошковима лечења шизофреније спроведене широм света показују широк опсег средстава које земље издвајају из укупног буџета здравства за лечење шизофреније. Она се крећу од 1,6 % до 2,5%. Међународне студије о трошковима лечења шизофреније закључују да су трошкови ове болести високи, зависни од здравственог система и локације као и да нематеријални трошкови *per se* већ оправдавају улагања у испитивања и развој нових начина лечења. Већина објављених радова сугерише да атипични антипсихотици имају бољи профил трошак-ефикасност од антипсихотика прве генерације. Сматра се да оланзапин, клозапинир и сперидон имају најповољнији профил трошак-ефикасност за лечење шизофреније.

**Кључне речи:** шизофренија, фармакономија, трошкови болести.

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## INTRODUCTION

Schizophrenia is one of the most serious psychiatric illnesses belonging to the group of non-affective psychoses. It is characterized by distortions of thought, perception, emotions and behavior. It is inherited poligenically. Various external factors contribute to the emergence of this disease, whilst the symptoms and the clinical manifestations are consequence of malfunctions in biochemical brain processes<sup>1</sup>. Twenty-four million people around the world suffer from schizophrenia<sup>2</sup>. Its prevalence is estimated between 0.3 and 1% worldwide, and its incidence is from 15.2 to 20.0 per 100,000 populations/year<sup>3-5</sup>. Schizophrenia is chronic illness associated with significant expenses which are imposed on both the health system, extended social community and family, as well<sup>6,7</sup>.

Treating schizophrenia is huge challenge for clinical doctors, due to its complex symptomatology and unpredictable, patient-dependent course of illness. The illness outlook is good in 40% of cases, extremely unfavorable in 40%, whereas in the remaining 20% it has moderately progressive course. The patients suffering from this illness have higher risk of comorbidity and social isolation, they have problems finding employment, while the death rate is double that of general population, which makes this illness one of the most expensive psychiatric illnesses<sup>8,9</sup>.

Discovery of the mechanism of action for the first antipsychotic drug 60 years ago opened a path to synthesis of new group of drugs with similar profile (antipsychotics of the first generation), which, together with psychotherapeutic and socio-therapeutic interventions were significant step forward in the treatment of schizophrenia. Thirty-five years later, many antipsychotics of the second generation have been synthesized, and turned to be as efficient as the conventional antipsychotics, but with significantly better profile of side effects and superior tolerance, offering wider range of possibilities for treating this illness<sup>10,11</sup>. Nevertheless, despite modern pharmacotherapy, 20-30% of patients have weak response to the therapy, 15-20% of the patients have relapses every year, while certain patients relapse when taking maintenance therapy<sup>12-14</sup>.

## SCHIZOPHRENIA AND ECONOMIC CONSEQUENCES

Cost of illness studies of schizophrenia conducted around the world show wide range of material resources that countries set aside from

their health budgets in order to treat schizophrenia<sup>15-18</sup>. They range from 1.6% to 2.5%<sup>19,20</sup>. According to the general conclusion of the analysis of several cost of illness studies of schizophrenia given by Knapp, these costs are high, dependent on the health system and location, and intangible costs per se already justify investment in research and development of new treatments<sup>7</sup>.

Results of the costs-of-schizophrenia study conducted by Mangalor and associates in England during 2004 and 2005, showed that total expenses were 6.7 billion pounds, where 2 billion pounds represent direct expenses. Out of 4.7 billion pounds set aside for indirect expenses, the largest part of 3.4 billion pounds was used for expenses due to productivity loss for the reasons of sick leave, unemployment and deaths connected to schizophrenia, while the expenses of the productivity loss of caregivers amounted to 32 million pounds. The expenses of patients' families and private care were 615 million pounds. The cost of criminal proceedings with the patients suffering from schizophrenia amounted to 1 million pounds. Around 584 million pounds was set aside for the benefit payments and administration costs connected to them<sup>15</sup>.

According to the cost-of-illness study conducted in Canada during 2004, total expenses connected to schizophrenia were 6.85 billion Canadian dollars. Total direct expenses were 2.02 billion Canadian dollars. Out of 4.83 billion Canadian dollars set aside for indirect expenses, the largest part (70% of total expenses) was spent to cover productivity loss due to morbidity. During 2004 there were 374 deaths connected to schizophrenia in Canada, which also contributed to the increase of the expenses in relation to this illness<sup>16</sup>.

According to the study of Carr and associates, Australian government set aside 1.45 billion Australian dollars during 2003 for the expenses of dealing with psychoses, including schizophrenia. The government set aside, on average, around 46,200 Australian dollars for a patient suffering from psychosis, where 27,500 Australian dollars were expenses due to productivity loss, 13,800 Australian dollars were expenses for hospital treatment and 4,900 Australian dollars were expenses for outpatient health care<sup>17</sup>.

In USA, according to the study conducted by Cloutier and associates<sup>18</sup>, economic costs of schizophrenia equaled 155.7 billion US dollars for 2013. Direct expenses were 37.7 billion US dollars, and indirect expenses were 117.3 billion US dollars. The largest part of indirect

expenses (72%) was in relation to unemployment and the productivity loss of caregivers.

### **ECONOMIC EVALUATION OF ANTIPSYCHOTICS RELATED TO THE TREATMENT OF SCHIZOPHRENIA**

Pharmacotherapy of schizophrenia is based on antipsychotic drugs. However, their effectiveness is limited, often connected with discontinuation of treatment, relapses and hospitalization<sup>21,22,23</sup>. Drug prescriptions appear to contribute little to total costs<sup>7,24,25</sup>, but drugs may influence hospitalization rates and productivity, thus becoming rather significant for the economics of schizophrenia<sup>26,27</sup>.

McEvoy<sup>28</sup> came to a conclusion that hospitalization costs decreased in the United States of America between 1991. and 2002. However, the costs of outpatient treatment and medication went up. The decrease of inpatient costs could be explained by changes of policy and availability of new drugs for treatment of schizophrenia. In fact, there was a trend to decrease number of psychiatric beds all round the world over the last few decades, as a result of reforms in mental health care concepts and practices<sup>29</sup>. However, in spite of that, the costs of hospitalization are still the main direct cost driver of schizophrenia. Limiting length of stay and decreasing probability of relapse reduce treatment costs of schizophrenia<sup>3,24,25</sup>. Adverse effects of these drugs can vary, primarily considering higher risk of extrapyramidal syndrome concerning the first-generation antipsychotics (FGA) and risperidone, metabolic syndrome with olanzapine and clozapine, hyperprolactinemia with risperidone and agranulocytosis with clozapine<sup>26,30,31</sup>.

If one takes into account limited productivity of pharmacological treatment of schizophrenia, which is associated with high costs of the disease and increasingly higher expenses for medicines by health systems, it is necessary to evaluate cost-effectiveness profile of antipsychotic drugs in order to allow an adequate choice of pharmacotherapy for patients, in line with the financial reality of health systems.

Majority of published papers suggest that atypical antipsychotics have more beneficial cost-effectiveness profile in comparison to the first generation antipsychotics. According to the study conducted by Santos and associates in 2016<sup>32</sup>, which evaluated cost-effectiveness of atypical antipsychotics in Brazilian public health system, it was found that olanzapine was domi-

nant over the other drugs. Nevertheless, validity of these study was not completely proven due to limited number of antipsychotic drugs included, but also due to the fact that quality of used data could not be checked.

Furthermore, randomized controlled study conducted by Davies and associates<sup>33</sup> showed that economic costs were lower and number of quality-adjusted life years gained higher when antipsychotics of the first generation were used in the therapy of schizophrenic population that was responding poorly to previous treatment, instead of atypical antipsychotics. Two more studies conducted in Great Britain came up with similar conclusions<sup>34,35</sup>.

However, the systematic review of literature related to cost-effectiveness analysis of head-to-head comparisons of antipsychotics in schizophrenic populations that encompassed 24 studies with data from 14 countries, showed that clozapine, risperidone and olanzapine were the most cost-effective in treating schizophrenia<sup>36</sup>.

Validity of existing literature data should be carefully checked in regard to the manner of selection of subjects, method of estimation of direct and indirect treatment expenses, as well as interests of financiers. Namely, pharmaceutical companies provide studies whose results show an undoubted advantage of new medicines being placed on the market, while the research groups financed by Ministries of health or certain bureaus and funds, generally emphasize apparently cheaper and older antipsychotics<sup>37</sup>. Not only pharmacoeconomic studies, but also numerous clinical studies that analyze the problems falling within the domain of pharmacoeconomics, were the basis for modern schizophrenia treatment guidelines which give advantage to newer antipsychotics, pointing out that there are differences even among these medicines. According to the literature search, pharmacoeconomic analysis related to schizophrenia treatment as well as the cost effectiveness study of antipsychotics used in therapy still have not been conducted in Serbia.

### **CONCLUSION**

Schizophrenia is chronic illness associated with significant expenses which are imposed on both the health system, extended social community and family, as well. International cost-of-illness studies on schizophrenia came to the conclusion that the costs are high, dependent on the health system and location and that the intangible costs per se already justify inve-

stments in research and development of new treatments. The majority of published papers suggested that atypical antipsychotics have more beneficial cost-effectiveness profile in comparison to the first generation drugs. Olanzapine, clozapine and risperidone are atypical antipsychotics that were generally found to be the most cost-effective in treating schizophrenia.

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