METHODOLOGICAL ASPECTS IN ESTIMATING THE COST-OF-ILLNESS FOR PATIENTS WITH RARE DISEASES

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Abstract: *Assessment of cost-of-illness and impact of rare diseases contributes to estimate the needs determined by rare diseases for the health care system. The main aim for allocating the necessary resources is to reduce the rare diseases effects for patients and their families, health care system and society, in general. The quantification of direct costs (medical and non-medical) and indirect costs generated by loss of productivity can hope to design a picture about the rare diseases impact. The estimated annual average cost per patient in this pilot study is about 15000 Euros. This value is under the European average cost generated by rare diseases, because the loss of productivity and the payment of caregivers are calculated based on the average salary in Romania. The new medical technologies are expensive and require a careful analysis that would create a balance between costs and outcomes in social and health care system.*

Rezumat: *Evaluarea costurilor asociate bolii şi a impactului afecţiunilor rare contribuie la estimarea nevoilor pe care le determină la nivelul sistemului de sănătate. Alocarea resurselor necesare va conduce la reducerea efectelor bolilor rare asupra bolnavilor şi familiilor acestora, sistemului de îngrijiri de sănătate şi societăţii, în general. Cuantificarea costurilor directe (medicale şi nemedicale), precum şi a celor indirecte generate de scăderea productivităţii contribuie la schiţarea unei imagini de ansamblu asupra impactului generat de bolile rare. Costul mediu anual estimat per bolnav în cadrul actualului studiu pilot este de aproximativ 15000 euro, ceea ce se situează sub media costurilor europene, fapt explicat mai ales prin calculul lipsei productivităţii şi a plăţii îngrijitorilor la domiciliu în funcţie de nivelul salariului mediu din România. Tehnologiile medicale noi, costisitoare necesită o analiză atentă, pentru crearea unui echilibru între costurile acestora şi rezultatele în domeniul social şi cel al sănătăţii.*

INTRODUCTION

Rare diseases are defined according to their prevalence (a rare disease affects less than five in 10,000 people in European Union).(1) The number of known rare diseases is between 6,000 and 8,000 and they affect 6-8% of the EU population claiming a major economic impact.(2) These conditions have important consequences for patients, their families and society, providing a real public health problem, by high morbidity and mortality, as well as a strong economic impact and burden of the disease.(3,4) It is useful to estimate the burden and the economic impact of the disease in order to understand the needs caused by rare diseases in the health care system. The necessary resources for rare diseases will reduce the effects that rare diseases have on patients, health and social system.(5,6)The cost-of-illness constitutes the value of the resources that are expended (medical and non-medical) or foregone (decrease or loss of productivity) as a result of a health problem and is calculated as the sum of the direct, indirect and intangible costs caused by the disease.(7)

PURPOSE

The goal is to generate a set of tools for the estimation of the cost-of-illness for patients diagnosed with rare diseases. The objectives of the study are: 1) generating a methodological framework for assessing health and social costs associated with rare diseases; 2) developing an appropriate and a common tool for cost evaluation; 3) assessing the costs-of-illness in a pilot study conducted on a population of patients diagnosed with rare diseases.

METHODS

The study regarding the estimation of the costs associated with rare diseases is based on a descriptive approach. The first phase of the study constitutes a review of the literature in this field in order to identify the main types of costs associated with the disease. These are the costs that can be estimated based on a questionnaire administered to patients with rare diseases. Based on a list of questions it was created a questionnaire structured in four key areas (socio-demographic and medical data, data regarding the access to health services, data regarding the loss of productivity in patient and their families, data regarding other costs associated with the disease).

The questionnaire was adapted according to the respondents, thus resulting in two questionnaires, one for patients with rare diseases, and the other for the families of children with rare diseases. The management of the developed quality control tools was made through their evaluation by five specialists. Each question was analysed in terms of accuracy of expression and the degree to which the respondents will understand it, and the relevance for the general purpose of the survey. The questions that were not relevant, that had the same meaning, or that generated ambiguous answers were eliminated or modified. In

the second phase of the study, the questionnaires characteristic for the study were applied along with questionnaires validated for health-related quality of life (EQ-5D-5L (8) - used with permission of EuroQol Group) on a group of 20 patients diagnosed with rare diseases. Data quality management was continued by comparing the results with the patients' medical records. There were also calculated the correlations between the costs of illness and self-perceived quality of life (figure no. 1).

Figure no. 1. Phases of research process
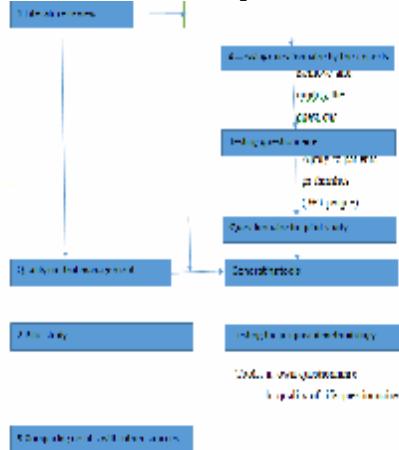
Cost-of-illness includes both direct costs (costs of resources used to treat the disease) and indirect costs (the amount of resources lost by disease).(9) In addition, cost-of-illness includes the intangible costs caused from pain, suffering, disfigurement, etc. that represent a highly subjective dimension.

The calculation of the intangible are omitted because it is very difficult to quantify the intangible costs in the monetary units.(10,11) The cost-of-illness was calculated by summing the direct and indirect costs:

Cost-of-illness = direct costs + indirect costs (figure no. 2), where:

Direct costs = medical costs (no. outpatient visits * average cost per visit + no. GP visits * average cost per visit + no. hospitalizations * average cost per hospitalization) + non-medical costs (transportation to the doctor / hospital + caregiver salary).

Indirect costs = average value of production * (no. days production lost because of illness + no. days production lost because of care giving).

**Figure no. 2. Main categories of costs-of-illness**
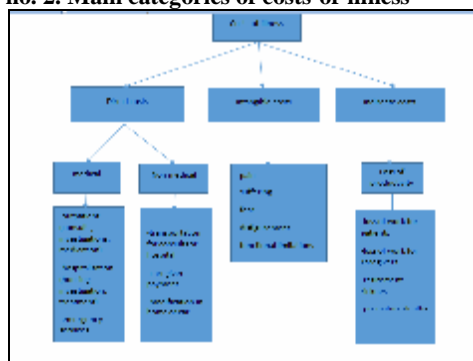
Statistical analysing plan for the pilot study includes descriptive statistical analysis of demographic data, of the data regarding the access to medical and social services and estimated costs. In addition we analyse the correlation between

the quality of life and the access to medical services. Data were analysed using SPSS 17.0.

RESULTS

20 patients with rare diseases were enrolled in the study, 17 adults and 3 children. The median age was 24 years, 12 patients were male. Most patients (17) lived in urban areas. More patients have a higher education level (12). All 20 patients are included in the National Program for Rare Diseases (NPRD). The average per year per patient cost financed by the NPRD for diseases witch are covered is between 8400 and 61,000 lei (according to current regulations) (figure no. 3).

Figure no. 3. Average of annual cost per patient of specific medication paid by National Program of Rare Diseases
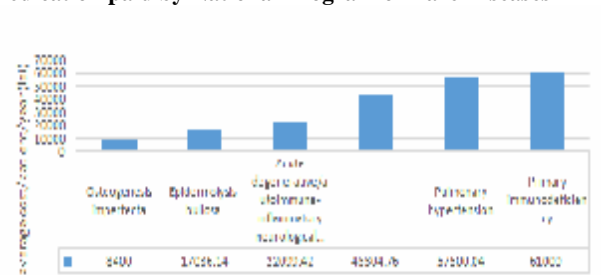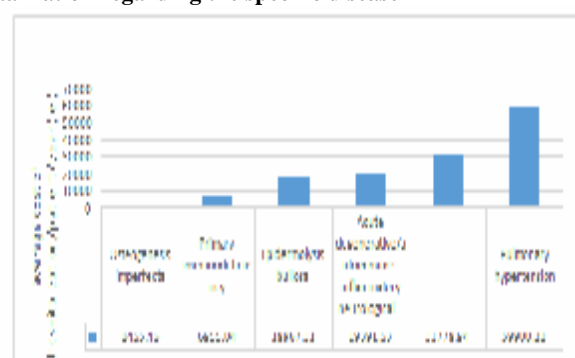

Source: National Health Insurance Agency, 2013

The median number of visits to the GPs is 8, and to the emergency services is 2, in the last year. The median number of hospitalizations was 3 in the last 12 months and the distribution of the number of days of hospitalization was between 0 and 83 days, with a mean of 17 ± 17.79 in the same period of time. The yearly average cost per patient for hospitalization was significantly different according to the patient's disease (figure no. 4).

None of the patients included in the study was not retired illness. The yearly average number of illness days of patients included in the study (their absenteeism or a family member) was 47.5 (between 0 and 135). The estimated yearly average cost per patient was 3,652.97 lei because the loss of productivity (taking into account an average salary of 1,615 lei in 2013). The average score of quality of life was 67.8% and was negative significantly correlated with the number of illness days in the last year ($p = 0.021$). It means that the number of illness days increased when the quality of life decreased, and vice versa.

**Figure no. 4. Average annual cost per patient of hospitalization regarding the specific disease**

Source: Health Insurance Agency Bucharest 2013

By adding all kinds of costs associated to the rare disease, both formal and informal, collected from the

questionnaires, the average annual cost per patient is 67,651.56 lei, yearly cost is different according to the group of diseases (figure no. 5).

Figure no. 5. Average annual cost-of-illness per patient in persons with rare diseases
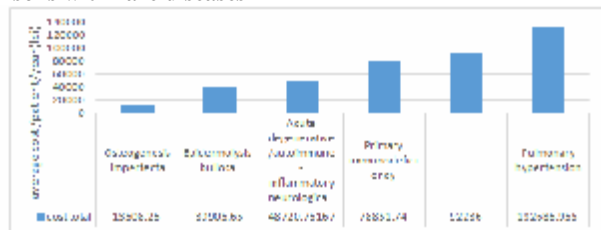
DISCUSSIONS

All patients involved in the pilot study are included in the NPRD as the selection process of the respondents was conducted in university medical centres. These patients generate higher direct medical costs, but intangible costs, as well as the costs of premature deaths will be lower. The access to an accurate diagnosis and therefore to a treatment specific for rare diseases is higher among the people from urban areas and among those with higher education. In Romania, the NPRD included in 2013 a total of 5,385 patients from the 19 groups of diseases legally accepted who received specific treatment, at an average cost of 37,905 RON per patient, every year.

The highest recorded average annual cost in the pilot study, through the PN was for primary immunodeficiency, according to the technical rules of national health programs.(12)

In our study, the average annual cost per patient is around 15,000 Euro, way below the European average cost. There were no differences between the costs of specific drug, which shows the harmonization of the treatment and its costs on a European level and the Romanian patients' access to appropriate therapy. The difference in costs was due mainly to indirect costs, lack of productivity and the fact that the payments of caregivers is calculated based on the average wage (307 euros in Romania in 2013, 6-10 times lower than in European countries where were conducted studies in order to estimate costs).(13)

CONCLUSIONS

Determining the costs-of-illness is a main factor in the decisions taken by people in key positions, knowing that the resources are limited. Estimating the burden of the disease shows that rare diseases are an important public health problem, because they represent a major cause of morbidity and mortality, with major repercussions on individuals, the health and social system. The decision-makers have the necessary means to create a balance between the costs and the results obtained in the social and health system. As new, and seemingly expensive medical technologies are being developed, it is important to assess the real and potential impact of rare diseases on both social costs and health outcomes.(14)

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