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IANUA: a regional project for the determination of costs in HIV-infected patients

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Abstract. HIV treatment is based on combined antiretroviral therapy (cART) which has substantially improved survival, thus resulting in an increase in patient life expectancy as well as in the cost of HIV-related medical care. Therefore, several cost effectiveness studies were implemented worldwide, with one specifically in the Liguria region (Italy), to compare the annual economic expense in this area for HIV services, and the related improvement in patients' health. The IANUA project is intended to implement both cost-effectiveness and cost-utility analysis, therefore data related to clinical indicators and perceived health status were collected, the latter using a questionnaire based on the EQ-5D-3L. Information about the antiretroviral drugs and the relative quantity that a patient withdraws from the hospital pharmacy every month were extracted from the regional "F-file". All data gathered were stored in the Ligurian HIV Network, a web platform developed by the DIBRIS - Medinfo laboratory. More than eight hundred questionnaires were collected, and data will be elaborated by economists and psychologists. The first statistical elaborations showed that, as expected, costs increased as the number of therapeutic lines increased. Moreover, the average annual costs for patients whose last CD4 values were below 200 cells/mmc corresponded to the maximum expense recorded, however, the cost for patients with final CD4 counts above 500 cells/mmc was not, as expected, the lowest found. This can be explained by the fact that stabilized patients, who had CD4 values below 500 cells/mmc, did not need very expensive care, while patients with CD4 counts above 500 cells/mmc improved their health status thanks to cART.

Keywords. Antiretroviral treatment, Cost effectiveness evaluation, HIV, AIDS, Data base reporting service in clinical environment, direct reuse of clinical data.

Introduction

According to the WHO (World Health Organization), 35.0 million people worldwide are currently living with HIV/AIDS, and an estimated 2.1 million individuals were newly infected with HIV in 2013 [1]. Ongoing HIV infections will continue to drive up population cost for HIV services, which are expected to continue to increase, partly due to HIV-infected patients' longer survival on combined antiretroviral therapies (cART) and the relative lack of success of HIV prevention programs [2]. Where possible, the cost of HIV treatment and care need to be reduced without reducing the quality of services. Therefore, cost effectiveness studies should be implemented to compare the annual economic expense for HIV services, and the related outcomes, intended as the improvement in patients' health. Consequently, a research project was carried out in the Liguria region, Italy, in order to quantify the regional expenses for HIV+ patients ("Indagine sull'Appropriatezza prescrittiva degli aNtiretrovirali Utilizzati nel pAziente con infezione da HIV" – IANUA) [3]. In details IANUA intended to compare the different cART therapies by analysing cost-benefit and cost-utility. Data were gathered from three infectious disease wards in the metropolitan area. Within this project, a significant effort for automatic data extraction and data treatment was set up. This effort was performed with the specific intended reuse of an already developed tool.

1. Material and methods

1.1 Materials

The technological effort in the IANUA project had the task of comparing the Liguria regional costs for the treatment of HIV-infected patients and the relative outcomes, in order to determine if the current mix of interventions represented efficient use of the allocated health resources. In this project, information regarding demographic characteristics, clinical parameters (viral load, intended as the HIV-RNA copies/mL, and CD4+ cell counts) and quality of life were collected laying the foundation for further cost effectiveness and cost utility analysis [4], [5].

Patients' quality of life was determined through the assessment of a standardized questionnaire based on the EQ-5D-3L score composed of five questions about the health status perceived by the patient, with a 3 choice answer, and a VAS rating scale - a vertical 20 cm visual analogue scale, ranging from 0 to 100, with 0 being the worst health state and 100 being the best. The information collected through the questionnaires was used to implement the statistical analysis, in order to evaluate the economic impact of cART and find out the main cost determinants. All data collected through the questionnaires were stored in a database called Biobanca, by means of a dedicated platform, the Ligurian HIV Network [6], [7]. This platform was developed by the DIBRIS Medinfo laboratory. Moreover, therapeutic information was also considered in regards to both costs and also depending on patient-perceived general health status. This information was extracted from the so-called "F-file", which is a document used by hospitals to periodically collect the costs incurred for the delivery of drugs directly to patients not hospitalized. Computer procedures to analyse this kind of file and record the data contained in it were developed. This program supplied the

Biobanca database with information about the antiretroviral drugs used and the relative quantity that a patient withdrew from the hospital pharmacy every month, with the respective dates.

1.2 Methods

Demographic and clinical information was required for all patients taking part in the study. Sophisticated engineering tools to support the reuse of data stored in medical records belonging to different medical structures were developed. In 2013, the Medinfo researchers designed a web service-oriented architecture (SOA) that would support the direct connection between the medical records of the departments involved in the Ligurian HIV Network and the platform, allowing the automatic transfer of data to the Biobanca database. To facilitate integration with other health care facilities, communication between the systems involved was based on the exchange of medical records mapped according to the standard Health Level Seven (HL7) Version 3 (v3) Clinical Document Architecture Release 2 (CDA R2). Two Ligurian hospitals were automatically connected to the platform: IRCCS AOU San Martino Hospital – IST and the Galliera hospital in Genova. For the first, a client application was developed which permitted automatic data extraction from the EHR, and conveyed it towards the Biobanca database. Actually, the hospital did not provide the whole database, but just three anonymous views related to patients' clinical data (with non-sensitive personal data content). Instead, for the Galliera hospital, clinical data was provided by an appropriate web service, in XML or JSON format. A client application that queries the service to obtain the interest data was developed. The main clinical parameters provided were laboratory results, i.e. blood sampling date, exam codes and names, units of measure, result values, range values. Personal data, such as birth month and year, birthplace, sex, hospital code and citizenship, were supplied for each patient. Once the Biobanca database was filled with data from both hospitals, a SQL Server Reporting Service (SSRS) was used to easily generate up-to-date reports from it.

2. Results

Data from the 2,235 patients involved in the IANUA project were saved in the Biobanca database, but only 888 submitted the questionnaire. In this paragraph we will only refer to these 888 patients. At present, the average age is 51.7 with a standard deviation of 9.2, with 333 patients in the range of 40-50 years and 343 in the range of 50-60, while the other ranges contains less than 100 patients.

The index of perceived health status measured by the visual scale is 70-80/100 (Fig. 1). The results of the EQ-5D-3L questions are summarized in Table1. Moreover, 45.2% of the patients are currently taking other drugs in addition to the prescribed treatment.

Since HAART costs are the major driver of total health care expenditure devoted to patients with HIV infection [8], [9], preliminary analysis focus on antiretroviral drugs costs (determined on the basis of the real costs incurred by hospital pharmacies). The results show that the average per patient annual HAART cost increases with more advanced HAART line and decreases with higher CD4+ cell count.

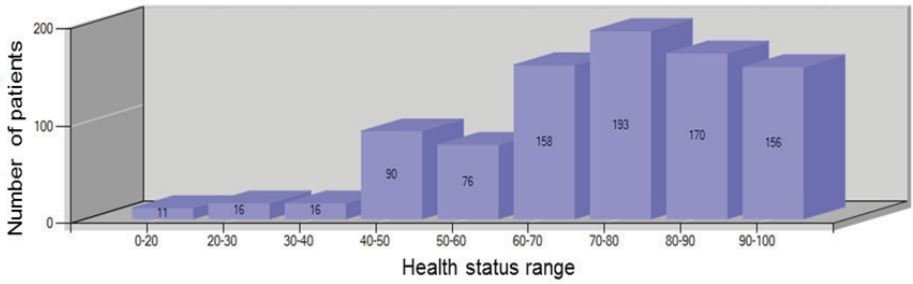

Figure 1. Distribution of the perceived health status

Analysis of the self-report questionnaires indicates that Health-Related Quality of Life (HRQoL), in our sample group, is not deeply affected by HIV/AIDS. The dimensions that are least affected are "mobility" and "self-care" while the major problem is "anxiety/depression" with half of the sample reporting moderate or high levels.

Table 1. Results of the EQ-5D-3L questions

	None (%)	Medium (%)	High (%)
Mobility problems	***82.4***	***17.4***	***0.2***
Self-care problems	***93.9***	***5.7***	***0.4***
Usual activities problems	***85.6***	***13.7***	***0.7***
Pain/Discomfort	***63.5***	***30.9***	***5.6***
Depression/Anxiety	***48.9***	***43.6***	***7.5***

Table 2 shows that patients in the first therapeutic line incurred minimum annual costs, and as the number of therapeutic lines increase, the costs also increase.

Table 2. Average annual costs per patient for different therapeutic lines

Therapeutic line	% Patients	Average annual cost
I	***4.4***	***€ 8751,74***
II	***7***	***€ 9066,16***
>II	***88.6***	***€ 9489,28***

The average annual costs per patient was calculated and differentiated into three groups according to the CD4 cell counts. The first group includes patients whose last CD4 values were below 200 cells/mmc. The average annual costs for patients belonging to this group is € 9959.98, which is the most expensive, as shown. This is exactly what was expected, since a CD4 cell count below 200 indicates a wretched state of health. The central group (CD4 range: 200-500) shows the lowest average value, € 9066.16, in accordance with the increase in CD4 cells, but the last group (CD4>500) behaves in an apparently unexpected way since the cost registered was € 9489.28. The central group includes stabilized patients, who did not need very expensive care, while the third group of patients improved their health status thanks to an intensive treatment. To determine if the difference between the averages of the three samples is significant, a t-test was performed. It showed that the difference between the

first group and the other two groups is highly significant, while the difference among the second and third group although still significant, is weaker.

3. Conclusion and discussion

The results shown in this paper are preliminary as further analyses of cost-benefit and cost-utility, will be completed within the period of the IANUA project. Several studies examined the advantages of the introduction of HAART therapies and have demonstrated its cost-effectiveness basing on QALY and life-years gained parameters [10]. In particular Lopez-Bastida et al in [11] reported results of a study which adopted EQ-5D questionnaires. Some of the authors were involved in previous studies [12] where the QALY value was calculated basing on CD4 count through the application of Markov model. The final results of IANUA project will be compared in future works with all the reported studies.

In the future, information regarding hospitalization costs will be gathered and an analysis of the effective total cost will be carried out at both hospitals.

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