Objective: to analyse the cost-minimization of the Allogeneic HSCT before and after the implementation of the SAE. Method: quantitative, evaluative and retrospective study, utilizing the tree of decision model to analyze the cost-minimization, being utilized variables related to the infectious during transplant and its respective costs. Results: it proved to be a higher cost in the year of 2006 - when the Systematization of Nursing Assistance (SAE) had not been established yet - if compared to the year of 2012. Conclusion: the analysis of cost-minimization appeared to be a lower cost for the allogeneic HSCT presented in 2012 (R$ 431,482,71), if compared to the ones accomplished in 2006 (R$574,688,22) suggesting that the SAE had cooperated on the cost reduction of the procedure, with an increasing cost of R$143,205,51 for the year of 2006.

Descriptors: Hematopoietic stem cell transplantation; Costs and Cost Analysis; Nursing Diagnosis; Nursing; Nursing Care; Health.

RESUMEN
Objetivo: analizar el costo-minimización del TCTH Alogénico antes y tras la implementación de la SAE. Método: estudio cuantitativo, evaluativo y retrospectivo, empleando el modelo del árbol de decisión para análisis del costo-minimización, siendo utilizadas variables relacionadas con las complicaciones infecciosas en transplante y sus respectivos costos. Resultados: se comprobó un costo más elevado en 2006 cuando no había sido implantada la SAE en 2012. Conclusión: el análisis del costo-minimización demostró un cost menor para el TCTH Alogénico aparentado en 2012 (R$ 431,482,71) en comparación a los costos del procedimiento, con costo incremental de R$143,205,51 para 2006.

Descritores: Trasplante de progenitores hematopoyéticos. Costos y Análisis de Costo. Diagnóstico de Enfermería; Enfermería; Atención de Enfermería; Salud.
INTRODUCTION

There is a global necessity of cost rationalization in Health because of the limited resources the Health Systems have and also the increasing enlargement and aging of the population, which must have a methodological basis that grounds the evaluation and point monetary values, as the clinical benefits associated to the decisions before the choosing of a determinate technology. In this context, the utilization of the Health Technology Evaluation (ATES) is legitimately a method that can assist the managers in making decisions about the incorporation of a new technology. In the field of Oncology, the necessity of making a better management is priority due to the high costs of the cancer controlling treatments.1

According to the International Agency for Research on Cancer of the World Health Organization, there were 14,1 million new cancer cases and a total of 8,2 million of deaths by cancer on the whole world in 2012. The prediction for 2030 is of 21,4 million new cases and 13,2 million deaths. In Brazil, the prediction valid for 2015 points to the occurrence of approximately 576 thousand new cancer cases.2

The hematopoietic stem cell transplantation (HSCT), also known as bone marrow transplantation, consists on the therapeutic procedure in which occurs the infusion of hematopoietic cells by intravenous route, with the objective to rearrange the destroyed bone marrow through chemotherapy procedure. This treatment is admitted when the hematologic toxicity is the limiting factor or when the pathological process reaches the bone marrow directly.3

The HSCT, besides being a highly complex procedure, also deals with high costs. In the United States of America the medium cost was estimated in US$193.000 per case, having as main limiting factors a small numbers of available beds to the accomplishment of the procedure and the high cost of new drugs for the treatment of the patient.4

There are three categories of HSCT: the autologous transplantation (the patient receives his/hers own bone marrow; this being, in most cases, a transplantation of minor complexity); the syngenic transplantation (transplant between twins, it is a rarer modality because of the low frequency of identical twins in the population); and the allogeneic transplantation (the patient receives the bone marrow of someone else, who can be a relative or not).3 When the donor is a patient’s relative it is called an allogeneic transplantation between relatives; when the donor is not a relative it is called an allogeneic transplantation between nonrelatives. In this second modality, there is a search for a compatible donor through the National Register of Bone Marrow Volunteer Donors (REDOME).5

The HSCT is regulated by the ministerial resolution of number 1.217/1999. In 2009 the Brazilian National System of Transplantation began to be a part of the National Marrow Donor Program, allowing foreign patients that need a donor to have access to the Brazilian stem cell banks. This measure broadens the possibilities of searching for donors through REDOME, reducing costs in the international search for our patients, which according to the Ministry of Health reaches 45% of the total searches.6

The HSCT presents a variable chart of toxicities related to the conditioning regime of extramedullary manifestation that may be potentialized by individual comorbidities, such as: mucositis, hemorrhagic cystitis, liver veno-occlusive disease, cardiotoxicity, among others.

Considering complications related to the period of bone marrow aplasia is severe pancytopenia, that if enduring has a high mortality rate and requires support measures such as growth factors, hemotherapy repositioning and antimicrobial coverage (febrile neutropenia and infections). As the main complication related to the graft is the graft-versus-host disease, and secondarily is graft failure. To each one of these medical charts/records, there is one or several support measure that will determine the final cost of the procedure.4

The Brazilian Association of Organ Transplantation showed that in the year of 2013, 1,813 bone marrow transplants were performed, being 1,144 autologous and 669 allogeneic, as presented by the Brazilian Transplant Registry (RBT). These numbers grew due to the campaigns carried out by the Health Ministry. Since 2003 the number of donors increased 16.000%. Before, the number of registers was of 35.000; currently this number represents about 3 million of registered donors according to the RBT of 2012.7

All of this process, from the search for a donor to the finalization of the treatment itself, causes a huge financial impact on SUS: the cost is of approximately 14 million reais for a hundred days period (approximate cost of the treatment period), once the estimated cost per patient by day submitted to the

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allogeneic transplant is of about R$2,236.00. It is worthy to mention that 95% of all transplants are performed in public institutions, so they are paid through SUS. 8

In the area of care management, SAE is a better way to operationalize the nursing process with the patient. It is a functional element, primordial to the nurse in the optimization and management of the nursing care, since it is based on technical and scientific knowledge resulting in individual assistance with excellence. 9

Although SAE is incorporated into the professional practice of some institutions, the difficulties for its implementation are related to the amount of human resources available to perform all the activities required by this methodology, which requires time for data recording and analysis, and shows that the nursing work processes are of great relevance to the Health Institution and to the SUS. 10

The use of SAE reduces the incidence and time of hospital admissions and creates a cost-effectiveness plan, which is of vital importance for the institutions that perform the transplantation of hematopoietic stem cells. 11 Resources for Health are scarce and the reliability of data analysis can be increased through the use of processes that favor planning, care evaluation and control of hospital costs. 12 It is from the knowledge of the costs of their interventions that nurses will effectuate positive changes, maintaining or generating balance among their quality, quantity and its costs. 13 On this subject, the following question can be raised: Can the cost of stem cell transplantation be reduced with the implementation of SAE?

**OBJECTIVE**

- To analyse the cost-minimization of the Allogeneic HSCT before and after the implementation of the SAE.

**METHOD**

This is a quantitative, evaluative and retrospective study, which used the economic evaluation through cost-minimization to identify if the cost of allogeneic transplantation was minimized after the SAE implementation. The costs of allogeneic HSCT were compared before and after the implementation of SAE in an oncology hospital located in the city of Rio de Janeiro. Two temporary cuts were made: one in 2006 when there was no SAE and another in 2012 already with SAE implemented, as will be described below.

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The choice of the institution was due to the allogeneic transplantation being a procedure of great complexity and the oncology hospital is one of the few that perform it in the State of Rio de Janeiro. The population studied was composed of all adult patients who were submitted to the HSCT in 2006 and in 2012 and underwent all treatment at the study site.

All the medical records were analyzed, making it a total of 158 medical records. The size of the population was justified by the following inclusion criteria: age range between 27 and 50, since it is the gap in which there is more productivity of the individual and whose exit from the labor market causes a great economic impact; the source of the transplant is the bone marrow, once they are the most used in the HSCT; and the type of transplantation is the allogeneic between relatives, since they are the ones performed more frequently in this transplant center and do not depend on the search for donors on the bone marrow banks.

Criteria were applied based on the clinical conditions of the patients, to standardize the sample, also selected those who presented the same patterns of complications/alterations, namely: same conditions of febrile neutropenia, similar infectious chart such as infection of the bloodstream, invasive fungal infection and pneumonias, the type of antibiotics and laboratory tests. After applying these criteria, the sample was composed of 14 records divided into two groups.

The first group consisted of seven medical records of the patients who performed allogeneic HSCT in the year of 2006, when it had not yet been implemented in the unit. The second group consisted of seven medical records of the patients who underwent HSCT in the year of 2012, after the implementation of SAE in the related sector.

In the selected sample characteristics, it can be observed that 57.1% of the total number of transplanted patients had Acute Myeloid Leukemia as their underlying disease, with an increase in 2012, which accompanies a worldwide trend.

The medical records of the patients admitted to the transplant unit who were submitted allogeneic HSCT in the years of 2006 and 2012 were analyzed to collect data on the assistance given to the transplanted patient.

The cost data were collected as follows: for both the year of 2006 and the year of 2012, the hospital administration system ABSOLUT was used, whose patrimonial rights

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were acquired since 2000, and is integrated with *Business Intelligence*, which organizes and cross-references the patients’ data regarding the diagnostic exams, drugs and supplies expended by the hospitalization unit.\textsuperscript{14}

Data on pharmacy prices and storage materials are stored in this system, ABSOLUT. Through it were made collections of data on the prices of medicines and consumables. The prices of the laboratory tests of 2012 were extracted from this same system, but the prices of exams from 2006 were extracted from the table SIGTAP of the SUS, because there were no archived data in the system referring to the years prior to 2008. Regarding the examinations of antigenemia for CMV (cytomegalovirus), serum levels of CSA (cyclosporine) and Tacrolimus, and Galactomannan, the outputs were extracted from the INCA laboratories, they remain the same since 2008. In the search for results of blood components and stem cells bags there were many difficulties, being there no record in the institute of the costs of concentrates of red blood cells, platelets and stem cells.

The preachings/lectures of the Ministry of Health, with INCA code, were also used to extract data on materials and drugs that had not been found in the ABSOLUT system. In the search for price data, difficulties arose due to the lack of a database that concentrated all items, both in the HSCT service and in the National Cancer Institute in general.

To unformatize the costs data relative to different years and with an interval of six years, the US dollar currency unit was used, which minimizes the great instability of the national currency at this period of time.

For the data relative to the price of the hour worked by the nursing professional, the Human Resources Department of the institution was consulted for the acquisition of the salary scale of the Ary Frauzino Foundation. The salary scale for science and technology is available on the website of this Ministry for public consultation. In the institution there are two distinct links: employees hired under the Consolidation of Labor Laws and the employees of the Ministry of Health, Science and Technology. The average salary for each table was calculated and then an average between the two results to get to the hour value of the nurses. The salary valuations used were the same for both 2006 and 2012, as there were no significant salary increases in this period.

The data collection was accomplished through an instrument developed for this purpose. It is an electronic form, developed in Excell\textsuperscript{®} software, composed of four spreadsheets for collecting data from the pre, trans and post phases of the HSCT and costs. Each of the three spreadsheets of the transplant phases mentioned above were subdivided into four parts, which are: a) Quantitative of the inputs used; b) Quantitative of the medicines used; c) Type and number of examinations carried out; d) Professional nursing-time used by the professional.

The fourth worksheet was used for the collection of data on costs of medicines, exams, supplies and the professional workforce for each year (2006 and 2012), attributing to them the corresponding values, once it is a comparative study between these two different moments. Six months were spent collecting data from the selected medical records of the years of 2006 and 2012, as well as cataloging data on electronic spreadsheet, price search and statistical treatment.

A database of the transplants performed was originated from the spreadsheets in these two periods and the results were divided into three parts: the first referring to information on cost items, the second on costs and the third on cost-minimization.

For the first part of the results, the following cost items were analyzed: material inputs, medicines and exams carried out for the patient, the amount and the time of nursing for each year of data collection (2006 and 2012) and, for each phase of the transplantation (pre-transplantation phase, trans phase, post-transplantation phase). The second part was divided into two sub-parts: the cost of transplantation in 2006 and the cost of transplantation in 2012; and the third part was the cost-minimization analysis of the transplantation carried out in 2006 (without the implementation of SAE) and the transplant performed in the year 2012 (already with the SAE implemented in the Service).

The cost of the transplant was calculated from the costs found for each cost item (inputs, medications, exams) plus the amount of time spent by the professional, calculated from his/her time worked. Adding the cost of the inputs, medicines and exams performed and the cost of labor, we obtained the total cost of the procedure for each year studied. It is noteworthy that, in this study, only direct costs were used.

The analysis of the data on the inputs, medications, exams and hours worked by the professional, as well as their costs, was performed through Descriptive Statistics. In the third part, for the analysis of the cost-minimization, the analysis model called the...
decision tree was used, through the software TreeAge Pro®, which belongs to TreeAge Software Inc., version 2014.

The study was approved by the Research Ethics Committee of the Federal University of the State of Rio de Janeiro, as the proponent institution, and by the Research Ethics Committee of the co-participating institution National Cancer Institute, under the CAAE research protocol 20869513600005285 and resolution on 02/06/14.

RESULTS

To perform the cost-minimization analysis of allogeneic stem cell transplantation with and without SAE implementation, the decision tree model was used and to compose it, data on the costs of transplantation in the years of 2006 and 2012. Data on the complications associated with HSCT, obtained from the available literature and data on the cost of treating the complications of HSCT.

Based on the data provided, the cost-minimization analysis of the allogeneic HSCT between relatives to understand what was the less costly option in the two years, once SAE did not exist in one and in the other it had already been implemented.

The cost-minimization analysis of Transplantation with the SAE in 2012 showed a lower total cost when compared to the cost of transplantation performed without this systematization. In order to evaluate the robustness of the cost-minimization analysis, a series of varied sensitivity analysis were performed. To do so, all the cost variables included in the cost-minimization calculation were modified by more or less 20% of their estimated base price.

The cost item that most impacted in 2006 was medicine, with a total of R$198,353.85. This is due to the high costs of medications and also the incidence of infections with treatments for febrile neutropenia (R$17,437.45), bacterial infection (R$4,211.76) and fungal infection (R$19,835.38). Patients undergoing HSCT are at high risk for complications, requiring from the nursing team a qualified, accurate and directed care to the demands of this group. An adequate provision of Health Care is directly related to the quality and quantity of available human resources.

The elaboration of SAE is one of the means available to nurses to apply their technical-scientific and human knowledge in patient care and to characterize their professional practice, collaborating with the definition of their role.

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The time spent with labor in 2006 was much higher than in 2012, but despite the studies in this dimensioning area, we know that quantitative is not everything. There are few studies in the nursing area that address the influence of clinical nursing protocols on the total costs of any treatment, either in public or private institutions. Some authors mentioned previously that carried out studies addressing this theme affirm that the use of the SAE methodology brings better results in the quality of the assistance and in the outcomes relative to the patients.

Knowing the impact of HSCT costs for the SUS and the necessity for more beds available for treatment, the effectiveness of this should be guaranteed through the planning of nursing work, as well as good cost management. Among the comorbidities studied in transplantation, it is known that the cost with the treatment of infections overtaxes the total cost of the procedure, besides requiring more nursing hours due to the complexity of the infected patient.

DISCUSSION

For the year of 2012, the cost of the nursing workforce was of R$305,483.60, being lower than it was in 2006 (R$324,406.55). This value for 2012 was also expressive and with more cost-effective results. The significance of this fact is to spend the nursing hours with conducts directed to the most frequent diagnoses of risk, thus working in the prevention of complications, which optimizes the clinical results and reduces total hospital costs. The measures of prevention of infections and the assistance for patients of this nature include, among others: the follow-up of protocols for febrile neutropenia, caution with the catheters, hand washing and maintenance of a protective isolation environment. It is also important to emphasize the importance of the education of patients and family members and health staff, in order to generate behaviors that aim to minimize the potential risks of infection.

We observed a much lower cost with drugs, R$53,866,10, as well as with exams, R$5,809.40. Regarding inputs, this was the only item that presented a higher cost compared to 2006 and is due to the investment in prevention techniques and the maintenance of protective isolation, as well as the investment in contact precautions, which justify this higher expense. However, if the cost of inputs is compared with the cost of...
The difference in costs between the two interventions results in the incremental cost (R$143,205.51). This amount could, for example, pay for another allogeneic HSCT or two autologous transplants. We can also observe that the weight of human resources in 2006 was the one that impacted the most in total costs, but it was not as cost-effective if compared to the results of the procedure in 2006, once it had higher morbidity and overall mortality rates were higher. The year of 2012 had an important magnitude in relation to human resources, which, related to the results of the transplant in 2012, we see not only less morbidity, but also better survival rates. In 2006, the complexity of the patients was higher, requiring more nursing hours.

Medication costs in 2006 had a greater impact than in 2012, with prolonged and costly treatments for fungal infection. The results did not show better effectiveness. Third, in the impact on total costs, we see expenditures on inputs in the year of 2012. Input expenditures can be interpreted in two ways: due to the great complexity of the patient who demanded a higher expenditure (in the case of 2006) or a justified consumption with measures for prevention of infection in the handling of the patient, as it was in 2012, with results of lower infection rates. It can be stated that the total cost of the first intervention and the total cost of the second intervention are not proportional to their respective outcomes, since their magnitude was different.

We can observe that in the sample studied the costs and the probabilities of the intervention were compared. If we consider the possibility of alternative use of the necessary productive resources (opportunity cost), one could think of more outpatient care, ambulatory transplantation, training and reform aiming to improve the service provided.

CONCLUSION

This study is a pioneer in economic evaluation relating SAE and stem cell transplantation. We sought to contribute with the knowledge on transplantation of hematopoietic stem cells costs, in a Federal Public Oncology Hospital, located in Rio de Janeiro. With the implementation of the Systematization of Nursing Assistance, it became possible to effectively apply the medicines for the treatment of infections, the second is much higher than the first.7

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nursing process in all its stages, and it was perceived its importance not only from the point of view of the health care of the patient undergoing transplantation, as well as from an economic point of view.

The scarcity of studies developed in the area of economic evaluation by nurses in Brazil was observed. The United States was the country in which most of the economic analysis papers developed by nurses were found. The experience of this work opens new horizons for nursing research in HSCT, regardless of the type, where several procedures and nursing protocols can be evaluated in a comparative way, calculating its costs and its effectiveness in service.

It is considered necessary, from the point of view of the public management, as well as the gain of the professional nursing area, the continuity of studies that seek the validation of the effectiveness of clinical protocols with a view to economic analysis. This study brings to light many necessities within the HSCT service, such as comparative studies in the area of dressings, cost of long-term follow-up of the patient with graft-versus-host disease, and other issues within the area of transplantation of relevance to SUS, in order to guide better technology, budget and reimbursement options.

The analysis of the cost-minimization of allogeneic HSCT showed that the cost with SAE implementation is lower than R$432,543.59 and more effective, which is an important data that legitimizes professional practice, whereas without SAE it is higher than R$584,858.49, presenting an important data for reflection on nursing work methodologies.

Some difficulties were faced in the construction of this study, such as the lack of up-to-date publications of data on institutions that perform transplants in Brazil, and especially the difficulty to obtain cost data at the institution that served as the field for the study. It is important to emphasize that other factors may have influenced the results, such as changes in conditioning protocols, and the greater availability of drugs with lower prices in the market. This study seeks to bring contributions to the literature on HSCT in Brazil, bringing cost data that no other center had previously done.

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