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# An Estimate of the Cost of Hepatitis C Treatment for the Brazilian Health System

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ABSTRACT

**Objectives:** Hepatitis C therapy in Brazil is expensive due to the cost of antiviral drugs and demands on medical resources. The objective of this study was to estimate the direct costs per patient of chronic hepatitis C therapy in a Brazilian setting. **Method:** A microcosting study from a public health system perspective. The costs included were those of antiviral drugs, secondary medicines, diagnostic tests, visits to physicians and other professionals, hospitalization, nurse, and pharmaceutical care. All costs were priced in 2010. The values were converted to US $ (2010). **Results:** The total direct cost of hepatitis C treatment per patient with interferon alpha (IFN) plus ribavirin (RBV) was US $982.25, with peginterferon alpha (PEG) 2a 180 μg plus RBV was US $10,658.08, and with PEG 2b 120 μg plus RBV was US $12,597.63, taking into account entire treatment according to Brazilian guidelines and assuming that all patients completed full treatment. The antiviral drugs are the most expensive element of the cost of treatment, totaling more than 40% of the medical costs of IFN plus RBV therapy and more than 88% of PEG plus RBV therapy. Calculating an average of 10,000 treatments per year, the total direct cost is US $90,346,772.39. According to the Ministry of Health, 90% of the annual total cost of hepatitis C treatment is accounted for by antiviral drugs. **Conclusions:** In Brazil, antiviral drugs are the most expensive component of hepatitis C treatment. The cost of follow-up and support to patients is minimal compared with the cost of antiviral drugs.

*Keywords:* direct cost, hepatitis C, hepatitis C treatment, interferon.



## Introduction

Infectious diseases are a very significant public health issue in Brazil, not only in terms of overall morbidity but also due to the financial burden and extra demands placed on medical resources [1–3].

Hepatitis C virus (HCV) infection is a serious public health problem as 80% to 85% of HCV carriers develop a persistent infection. Cirrhosis, end-stage liver disease, and hepatocellular carcinoma are the most significant clinical consequences of chronic HCV infection [4]. Moreover, patients with chronic HCV infection require periodic ambulatory care to monitor and treat their condition. As a result, studies show that patients with chronic HCV infection [5] consume a substantial and escalating amount of health care resources.

Treatment for 24 or 48 weeks with interferon alpha (IFN) or peginterferon alpha (PEG) is recommended for people with HCV infection, according to viral and clinical characteristics. The primary aim of treating chronic hepatitis C is to clear HCV, in order to improve quality of life and reduce the risk of cirrhosis and hepatocellular carcinoma [6].

In Brazil, the public health system provides treatment for chronic HCV infection, including the use of IFN, PEG, and ribavirin (RBV). In 2007, the amount allocated to drugs in the Brazilian Ministry of Health budget was 10.7% and the specialized component of pharmaceutical services accounted for 42% of this expenditure [7]. Another study revealed that Brazil's national system to treat hepatitis C had an annual budget of US $14,553,293.90 in 2002 and US $31,633,149.41 in 2007 for medicines [8].

The treatment of HCV infection is expensive and almost 50% of all patients who undergo this treatment are not cured, representing a low cost-effectiveness ratio. The treatment can cause many side effects such as flu-like symptoms, fatigue, hemolytic anemia, neutropenia, depression, irritability, concentration loss and memory disturbances, skin irritation, and weight

Conflicts of interest: The authors have indicated that they have no conflicts of interest with regard to the content of this article.

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http://dx.doi.org/10.1016/j.vhri.2012.10.001

loss [9]. These side effects are the most significant obstacle to adherence [10].

Available data indicate that patients who are adherent and receive at least 80% of their total PEG and RBV doses for at least 80% of the duration of treatment have significantly higher rates of sustained viral response (SVR) when compared with patients with lower levels of adherence [11]. Studies show that patients are more likely to adhere to and complete therapy when there is ongoing support by a clinical team [12].

In a systematic review of studies of treatment of chronic HCV infection in Brazil, the rates of discontinuation varied between 4.5% and 44.4%. Meta-regression to evaluate the association between rates of no SVR and rates of noncompletion found a linear association and demonstrated that an increase of 10% in the discontinuation rate decreased SVR by 4.1%. According to this analysis, discontinuation of treatment is a major reason for the observed differences in rates of SVR in clinical settings compared with clinical trials [13].

In view of the fact that the rate of treatment discontinuation is indirectly related to service organization, this study aims to estimate the cost of chronic HCV infection therapy in a Brazilian setting from the perspective of the Brazilian National Health System. The subject of this study was a group of patients treated in a specialist public health center for HCV infection, cared for by a multidisciplinary team in accordance with Brazilian guidelines.

## Methods

A microcosting study from the perspective of the Brazilian public health system was carried out to identify the direct cost of treatment per patient. The study included the cost of antiviral drugs, treatment of side effects, diagnostic tests, the administration of injectable drugs, outpatient visits to specialist physicians and other professionals, and hospitalization due to treatment. These costs were estimated taking into account the entire treatment in accordance with Brazilian guidelines and assuming that all patients completed full treatment.

### *Antiviral Drugs*

The antiviral drugs and the duration of treatment were estimated according to Brazilian guidelines [14], and the costs of IFN, PEG, and RBV were those used by the Ministry of Health in 2010. These drugs were purchased through a public bidding process organized by the Ministry of Health.

### *Treatment of Side Effects*

The drugs used by patients to control side effects and their duration of use in the HCV infection therapy were identified from the prospective cohort study that was carried out in a specialist public health center in Florianopolis between 2005 and 2008 with 111 patients. A multidisciplinary team monitored patients weekly. Data were collected by a pharmacist who monitored patients [15].

The drugs used to treat the side effects resulting from HCV infection treatment were divided into two groups. The first included epoetin alpha and colony-stimulating factor for the control of anemia and neutropenia. The second group included other drugs to control side effects such as fatigue, headache, myalgia, rigors, fever, nausea, insomnia, and depression. The costs of epoetin alpha and colony-stimulating factor are based on Ministry of Health figures. The costs of others drugs are based on figures from the municipality of Florianopolis.

### *Diagnostics Tests*

The diagnostic tests for HCV infection were identified according to Brazilian guidelines [14]. The diagnostic tests were divided into initial tests and monitoring tests. The initial diagnostic tests included blood cell count, platelet count, alanine transaminase, aspartate transaminase, protronbin time, bilirubin, albumin, creatinine, uric acid, fasting glucose, thyroid–stimulating hormone, anti-HIV, antigen of the hepatitis B virus, beta human chorionic gonadotropin (women), liver biopsy, HCV genotyping, HCV gene quantitative for patients and use of PEG, and qualitative HCV. The follow-up diagnostic (monitoring) tests included complete blood cell count, platelet count, alanine transaminase, aspartate transaminase, creatinine, thyroid-stimulating hormone, HCV qualitative, and HCV quantitative [14]. The cost of diagnostic tests was taken from the Ministry of Health's database [16].

### *Administration of Injectable Drugs*

According to Brazilian guidelines, all patients undergoing HCV infection treatment should have medication administered in specialist clinics [17]. Therefore, it was assumed that all patients underwent the administration of injectable drugs in specialist clinics and the cost of this procedure was taken from the Ministry of Health database [16].

### *Outpatient Visits to Specialist Physicians and Other Professionals*

Visits to specialist physicians for routine follow-ups were estimated according to Brazilian guidelines [14]. Nursing care was calculated according to the frequency of the administration of injectable drugs. Pharmaceutical follow-ups were calculated monthly during the period of treatment. Outpatient visits to other professionals were estimated by using the prospective cohort of patients [18]. The cost of outpatient visits to physicians and other professionals was taken from the Ministry of Health database [16].

### *Hospitalizations*

The number of hospitalizations associated with HCV infection treatment was identified in a retrospective cohort [18]. The data were identified from the medical records of 188 patients who received treatment between 2003 and 2006 at a specialist clinic in Florianopolis. The cost of treating each patient was calculated according to the procedures described on the patient record. The cost was taken from the public health system database for hospital procedures [16]. The average cost of hospitalization per day was calculated by dividing the cost of all hospitalizations for full-time care by the number of days of hospitalization.

Our methodological approach set out to 1) identify the resources used, b) estimate costs from a public health system perspective, c) calculate the cost per patient, and D) calculate the Ministry of Health's estimated expenditure.

All resources identified were multiplied by the probability of being used by patients. The sum of the total costs is equivalent to the total direct cost taking into account all patients who received full treatment. All costs were based on prices from 2010. The figures were converted to US $ (2010), R $1.00 = US $0.57, according to the exchange rate on July 30, 2010 [19].

Data on the number of patients with HCV infection in Brazil between 2000 and 2009 were compiled according to the epidemiologic database [20]. The number of patients who have undergone HCV infection treatment in Brazil was estimated according to the number of units of IFN and PEG distributed by the Ministry of Health. By taking the number of patients diagnosed and treated annually in Brazil, we can estimate the annual budget to treat patients with HCV infection in Brazil.

## Results

### Antiviral Drugs

According to Brazilian guidelines for treatment-naive and genotype 1 patients, the recommended treatment is PEG 2a 180 μg or PEG 2b 1.5 mg/kg, administered subcutaneously once a week, in conjunction with RBV 1000 mg/day for patients weighing less than 75 kg or RBV 1250 mg/day for patients weighing 75 kg or more, for a period of 48 weeks if patients present an early virologic response (EVR) (negative polymerase chain reaction–HCV or drop of 2 logs in viral load from baseline) in week 12 of treatment. Patients co-infected with HCV-HIV may undergo the same therapeutic regimen for a period of 48 weeks regardless of genotype [14].

Naive patients with genotype 2 or 3 are treated with IFN 2a or 2b 3MU administered subcutaneously three times a week in conjunction with RBV 1000 mg/day for patients weighing less than 75 kg, or RBV 1250 mg/day for patients weighing 75 kg or more, for a period of 24 weeks [14].

Brazilian guidelines, revised in 2011, state that all relapse or nonresponder patients to previous HCV infection treatment can undergo a second course of treatment with PEG plus ribavirin for 48 weeks, irrespective of genotype. They also state that patients with genotype 2 or 3, and with cirrhosis or a Metavir score of F3 or F4, can undergo treatment with PEG plus RBV. Furthermore, there is a provision for 72 weeks of treatment for those patients who only obtain a negative polymerase chain reaction–HCV or a drop of 2 logs in viral load from baseline in week 24 of treatment [17].

The cost of antiviral drugs per patient to complete the treatment is US $303.29 for IFN, for 24 weeks of treatment; US $9447.68 for PEG 2a 180 μg and US $11,387.23 for PEG 2b 120 μg, for 48 weeks of treatment.

### Treatment of Side Effects

For treatment with PEG, the prevalence of the use of epoetin alpha was 31% with a range of use between 1 and 39 weeks. The median dose per week was 14,000 UI (10,000–42,500). The prevalence of the use of the colony-stimulating factor was 20% with a range of use of between 1 and 41 weeks. The median dose per week was 300 UI (300–525). As IFN treatment is for 24 weeks, half of this use was estimated. Therefore, the cost of epoetin alpha and colony-stimulating factor for PEG treatment is US $316.01 and for IFN treatment is US $158.00.

Analgesics and antidepressives are the medications most commonly used for treating side effects. The cost of these drugs is US $3.39 for PEG treatment and US $1.69 for IFN treatment.

### Diagnostics Tests

The cost of initial diagnostic tests for IFN treatment is US $260.23 and for PEG treatment is US $356.26. The cost of follow-up diagnostic tests for IFN treatment is US $91.02 and for PEG treatment is US $249.69.

### Administration of Injectable Drugs

For injectable drugs it was assumed that all patients underwent this treatment in specialist clinics three times a week for 24 weeks for treatment with IFN plus RBV and once a week for 48 weeks for treatment with PEG plus RBV. The cost of administering injectable drugs for IFN treatment is US $25.86 and for PEG treatment is US $17.24.

### Outpatient Visits to Specialist Physicians and Other Professionals

It was estimated that there were at least five visits to a physician for treatment with IFN plus RBV and seven for treatment with PEG plus RBV. The costs were US $28.50 and US $39.90, respectively.

Other patient referrals for treating side effects during antiviral therapy included dermatology, nutrition, and psychiatric care. The costs for IFN treatment and for PEG treatment were US $1.30 and US $2.62, respectively.

The cost of pharmaceutical care for IFN treatment was US $21.55 and for PEG treatment was US $43.09. The cost of nursing care for IFN treatment was US $86.18 and for PEG treatment was US $172.37.

### Hospitalization

The prevalence of hospitalization in groups undergoing PEG treatment was 4.3%, at an average cost of US $231.62. The total cost of hospitalization per patient for IFN treatment was US $4.93 and for PEG treatment was US $9.86.

### Total Annual Budget

The total direct cost of HCV infection treatment with IFN plus RBV was US $982.25, with PEG 2a 180 μg plus RBV was US $10,658.08, and with PEG 2b 120 μg plus RBV was US $12,597.63 (Table 1). The cost of treatment with PEG plus RBV was 10 times the cost of treatment with IFN plus RBV.

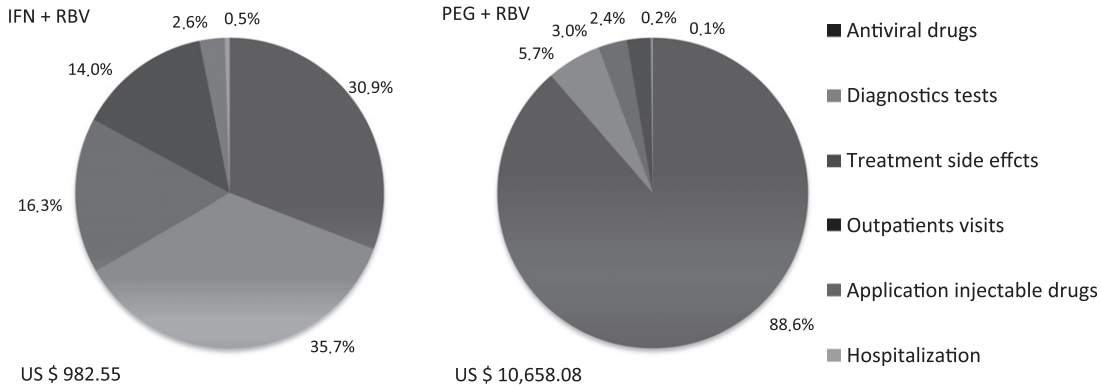


**Fig. 1 – Percentage of total direct cost for treatment of hepatitis C with interferon alpha plus ribavirin and peginterferon alpha 2a 180 μg plus ribavirin. IFN, interferon alpha; PEG, peginterferon alpha; RBV, ribavirin.**

The cost percentage is shown in Figure 1. Antiviral drugs are the most expensive category in the treatment cost, amounting to 30.9% of medical costs in IFN therapy and 88.6% in PEG therapy.

According to data from the Ministry of Health, between 2007 and 2009, 10,000 patients were being treated per year; 21% of these treatments were carried out with IFN plus RBV, 43% with PEG 2a 180 μg plus RBV, and 36% with PEG 2b plus RBV.

Given an average of 10,000 treatments per year and our estimate of costs for HCV infection treatment, the total direct cost per year was US $93,243,937.00. The cost of treatment with IFN plus RBV was US $2,062,725.00, with PEG 2a 180 μg plus RBV was US $45,829,744.00, and with PEG 2b plus RBV was US $45,351,468.00.

The costs were estimated assuming that all patients received complete treatment. Given that the range of discontinuation of therapy was between 4% and 44%, the total costs were reduced to US $91,379,058.26 and US $72,730,270.86 respectively, when discontinuation occurs at 24 weeks with PEG and 12 weeks with IFN. Treatment discontinuation, however, can lead to disease progression and an increase in costs.

## Discussion

### *Cost of Antiviral Drugs*

The cornerstone of therapy is the use of injectable PEG preparations. They are expensive and carry the risk of severe side effects and not all patients benefit from the treatment [21]. Data from Brazil corroborate this. The major cost component of HCV treatment is antiviral drugs. We found a great difference between the total costs of treatment with IFN plus RBV compared with PEG plus RBV (10 times higher). This could be around 31 times higher when compared with the cost of antiviral drugs.

The high cost of antiviral drugs justifies the use of guidelines to define the criteria to treat patients. Only those patients who present characteristics that are more likely to result in successful treatment should undergo this therapy. Therefore, further cost-effectiveness analyses are necessary, in particular subgroup analyses such as genotype and disease evolution.

### *Treatment of Side Effects*

If we include costs of side effects of drugs, professional pharmaceutical and nursing care (excluding specialist physicians), and hospitalization in the cost of the treatment, the total cost is US $165.93 for IFN treatment and US $331.85 for PEG treatment.

Side effects are the most significant obstacles to adherence [10]. Managing HCV infection treatment side effects is crucial to maintaining or improving adherence and successfully concluding treatment [12,22]. Preventing or correcting a therapy complication can increase the likelihood of adherence for patients and may improve virologic response rates [23].

The most frequent reasons for withdrawal are depression or an inability to tolerate side effects. Treatment cessation for neutropenia, anemia, or thrombocytopenia is infrequent, although many patients require dose reduction during treatment [10,24,25].

In Brazil, the number of patients who discontinue treatment because of side effects is between 4% and 44% [13], and therefore it is very important that patients undergoing HCV infection treatment are followed up and side effects are managed.

The most expensive side-effect control is epoetin alpha and colony-stimulating factor for the control of anemia and neutropenia. Although these agents are expensive, their use has increased in clinical settings to enable patients to continue their PEG plus RBV regimen and to sustain the RBV doses needed to maximize chances of SVR [22].

We found that 31% of the patients were treated with epoetin alpha and 20% with colony-stimulating factor. In another study, however, these figures were lower; 9% to 17% of the patients receiving PEG were also receiving granulocyte colony-stimulating factor or epoetin alpha [10].

Other drugs to control side effects are cheaper in comparison to granulocyte colony-stimulating factor or epoetin alpha and have advantages when used correctly as they can improve the likelihood of completing the therapy.

### *Diagnostic Tests*

Monitoring should include examination, determination of HCV RNA levels, verification of adherence, and assessment for side effects. Clinical and virologic monitoring should be conducted at intervals ranging from once a month to once every 3 months [12]. Hematologic monitoring is recommended for detecting anemia, neutropenia, or thrombocytopenia. Determination of thyroid-stimulating hormone is also recommended for identifying hyper- or hypothyroidism. Close monitoring for clinical signs of depression, with appropriate intervention, is of particular importance [25]. Tests such as genotyping and viral load can help estimate the likelihood of antiviral response and determine the duration of therapy, and other tests should be carried out for baseline values to monitor for potential side effects from therapy.

Monitoring of antiviral therapy is essential to maximize benefit and ensure that complications that might interfere with outcomes are prevented. Despite the fact that initial and follow-up diagnostic tests are very important, we know that in Brazil some patients have difficulty accessing them.

Diagnostic tests represent only 5.7% of the total direct cost of treatment with PEG plus RBV and 35.7% of the total direct cost of treatment with IFN plus RBV. This difference is due to the considerable contrast in price between these antiviral drugs; however, follow-up tests are cheaper for treatment with IFN plus RBV than for treatment with PEG plus RBV.

Moreover, another important reason for monitoring treatment is EVR. Clinical studies have shown that patients not achieving EVR by 12 weeks of treatment, defined as at least a 2-log reduction in HCV RNA levels, have only a small chance (<3%) of achieving SVR at the end of a full course of therapy [22,25,26].

This “12-week stop rule” is particularly important for patients with genotype 1, who typically require a 48-week course of therapy. In genotype 1 patients failing to achieve 12-week EVR, discontinuation of therapy is recommended. This not only prevents the patient from suffering from subsequent side effects but also generates considerable cost savings [25]. Economic analyses have shown reductions in the cost of lifelong antiviral drugs of about 45% with the use of the 12-week stop rule in patients receiving PEG plus RBV [10].

Another significant follow-up that many services and patients do not receive is the virologic assessment at the end of therapy. This follow-up is essential to check the effectiveness of the treatment, to evaluate the service, and for epidemiological data and the management of health care services.

### *Administration of Injectable Drugs*

IFN plus RBV is administered three times a week; therefore, its cost is higher in comparison to PEG plus RBV (once a week). The administration of injectable drugs is very important as many patients do not have the ability to administer these drugs themselves. Moreover, some patients do not have an adequate place to store drugs at home.

One advantage of administering injectable drugs in specialist clinics is the ability to control the allocation of antiviral drugs; this is especially the case for PEG 2a where doses are calculated

according to patient weight. A study in a specialist clinic for following up hepatitis C patients in Brazil (Rio Grande do Sul State) showed savings of R $1,300,000 a year (approximately US $600,000) as a result of controlled distribution of antiviral drugs to 395 follow-up patients with genotype 1 chronic hepatitis C [27].

### Outpatient Visits

The guidelines for HCV infection treatment in Brazil state that specialist physicians should care for all patients. During treatment other physicians are necessary because of side effects. Moreover, pharmaceutical follow-up is necessary to provide support to therapy and improve rates of adherence. Nursing staff members are responsible for administering injectable drugs and providing orientation about continuous follow-up.

Service provision by these professionals is included in the direct cost. Within the public health system in Brazil, however, it is very difficult for patients to access all these professionals. It is important to note that for therapy with PEG the cost of providing multidisciplinary care is less than 2% of the total direct cost of treatment.

The total therapy cost in the German context for IFN plus RBV is €16,433 and for PEG plus RBV is €25,028. Outpatient visits plus laboratory tests cost €355 and €382, respectively, which also represents around 2% of the total cost of treatment [28].

Studies show that patients are more likely to adhere to and complete therapy when there is ongoing support by a clinical team [12]. A multidisciplinary approach to supplement the role of the physician can enhance patient education, and can include family, nurses, pharmacists, nurse practitioners, and physician assistants [22]. The pharmacy, for example, can facilitate adherence by the use of pill organizers, accessible refills, and reminders and by identifying adverse events [11,22].

Follow-up of patients should be carried out in specialist clinics. Specialists have greater knowledge of current guidelines for treating HCV infection and are better trained to meet the needs of patients in relation to appropriate dosing, follow-up, and education, as well as being more capable of managing nonresponders, nonadherence, and side effects [25].

Ideally, a multidisciplinary team including experts in addiction medicine, psychologists, and psychiatrists should care for patients. Physicians must carefully weigh up the potential benefits and risks of therapy for each individual, deciding on the best predictor of treatment response.

Patient adherence to prescribed antiviral therapy enhances SVR rates [13] and therefore the possibility of preventing advanced liver disease [24,26]. Available data indicate that patients who are adherent and receive at least 80% of their total PEG and RBV doses for at least 80% of the duration of treatment will have significantly higher rates of SVR than do patients with lower levels of adherence [11].

Patient education is the key to adherence. The prescriber or other health care professional should assess the patient for comorbidities or contraindications to therapy. Implementation of system-wide patient education programs on all aspects of HCV, and drug therapy in particular, can maximize benefits of available therapies and help health plans achieve optimal results with the limited resources available [29]. Other measures that may improve adherence are frequent clinic and telephone follow-ups, visits and access to support groups, printed information, and self-monitoring devices [11].

It is important to be able to discuss the probability of cure before starting treatment, and how this relates to the ability of the patient to tolerate and complete the proposed course of treatment. Patients must be informed of the potential side effects of interferon-based therapies, how frequently they occur, their severity, and how they can be managed. Optimism should be emphasized, with assurances that most side effects, such as interferon-related depression, can be managed by dose reduction or other measures without the need to discontinue therapy [22].

### Hospitalization

The frequency of hospitalization is relatively low and is related to side effects as a result of HCV infection treatment. Because of the length of treatment and the frequency of side effects, the cost of hospitalization with PEG plus RBV was more expensive than with IFN plus RBV. Adequate follow-up and early care of side effects can prevent hospitalizations. This demonstrates the importance of patient follow-up by a multidisciplinary team.

A study using inpatient data from the Health Care Cost and Utilization Project, outpatient data from the National Ambulatory Medical Care Survey, and drug data from the Verispan Source Prescription Audit analyzed the recent growth in the use of health care resources among HCV infection patients by age group, and found average annual increases of 25% to 30% for hospitalizations, charges, hospital days, and physician visits [5].

### Total Estimated Budget

This is a preliminary study based on data from a sample of patients in one particular state in Brazil. Costs in other states may differ. However, using this data as a sample, the estimated budget to treat 10,000 patients was calculated at more than US $90 million, with antiviral drugs alone representing 88.2% of the total cost. The cost of follow-up and support to patients is minimal compared with the cost of antiviral drugs. In the case of the Brazilian public health system, savings could be made by providing adequate follow-up to patients undergoing HCV infection treatment. First, savings in resources could be made, resulting in improved cost-effectiveness. Second, further treatment could be avoided. Third, adequate follow-up may reduce hospitalizations and adverse events rates. Further analyses, however, are needed to calculate these savings.

Despite what is stated in the Brazilian guidelines, there are barriers to providing adequate follow-up related to the different responsibilities of government authorities. The Ministry of Health funds antiviral drugs while the funding of care and follow-up, including diagnostic tests and outpatient visits, is the responsibility of municipal governments.

Greater identification and effective treatment of HCV-infected patients, which would also reduce future HCV-related costs, can be facilitated by well-planned education programs for primary care providers. Furthermore, specialists are able to better ensure effective treatment and follow-up. Implementation of methods to ensure optimization of therapy can help attain therapy goals and reduce long-term treatment costs. These include measures to enhance adherence to therapy, close monitoring, and use of the 12-week stop rule. Enlisting the services of a specialist pharmacy is another way of maximizing the efforts of health planning to help patients achieve SVR, reducing long-term complications [25].

The present study has some limitations. The resources used were estimates from different studies in the state of Santa Catarina. The costs are exclusively based on the Brazilian National Health System's database and reflect the Brazilian health care system. We did not take into account expenditure directly on the part of the patient or private health plans. Some figures from the public health system include only the cost of procedures and not the monthly cost of physicians' salaries, for example.

We cannot guarantee that the drugs cost for the treatment of side effects obtained from the municipality of Florianopolis is representative of the country. The data, however, were taken from a specialist clinic for HCV infection treatment.

**Table 1 – Total direct cost (US $) of treatment for hepatitis C per patient with interferon plus ribavirin (IFN), peginterferon 2a 180 μg plus ribavirin (PEG 2a), and peginterferon 2b 120 μg plus ribavirin (PEG 2b).**

| | IFN | PEG 2a | PEG 2b |
|---|---|---|---|
| Antiviral drugs | 303.29 | 9,447.68 | 11,387.23 |
| Epoetin alpha | 110.06 | 220.13 | 220.13 |
| Colony-stimulating factor | 47.94 | 95.88 | 95.88 |
| Other drugs | 1.69 | 3.39 | 3.39 |
| Initial diagnostics tests | 260.23 | 356.26 | 356.26 |
| Follow-up diagnostic tests | 91.02 | 249.69 | 249.69 |
| Injectable drugs application | 25.86 | 17.24 | 17.24 |
| Visits to physician specialist | 28.50 | 39.90 | 39.90 |
| Visits to nutritionist | 0.20 | 0.41 | 0.41 |
| Visits to psychiatrist | 0.45 | 0.91 | 0.91 |
| Visits to dermatologist | 0.65 | 1.30 | 1.30 |
| Pharmacotherapeutic follow-up | 21.55 | 43.09 | 43.09 |
| Nursing care | 86.18 | 172.37 | 172.37 |
| Hospitalization | 4.93 | 9.86 | 9.86 |
| Total | 982.25 | 10,658.08 | 12,597.63 |

Other limitations are incomplete records, which may underestimate the use of resources. For some resources we assumed the same proportion of cost between PEG and IFN treatments. It was also difficult to obtain certain information from the State Health Department, such as hospitalization data.

We included only direct medical costs. We have not included costs of transport, reduced productivity, or absence from work.

Brazil does not have a homogenous pricing reference for complementary expenses with direct costs. For example, amounts attributed to the treatment (or follow-up) of patients with chronic HCV infection may differ when considering routine treatment in a reference clinic in a major city as opposed to a rural practice.

It is known that the rate of compliance to guidelines by health care providers in Brazil is low. Patients dependent on the public system have difficulties in accessing exams, drugs, and appointments with physicians. However, private health care patients are monitored through closely followed procedures and individual follow-ups. From a public health system perspective, it is important to note that diseases cannot be cured by the simple distribution of medication. It is necessary to improve the rates of cure to achieve more efficiency in the system.

Despite the limitations, there are merits to our approach, as pharmacoeconomic analysis must be adapted to the local reality. Furthermore, we are not aware of another study that collects data on the direct cost of treatment of hepatitis C in Brazil from a public health perspective.

## Conclusions

According to the Ministry of Health figures, 90% of the annual total cost of hepatitis C treatment is spent on antiviral drugs. The cost of follow-up and support to patients is minimal compared with the cost of antiviral drugs. In the case of the Brazilian public health system, savings can be made by providing adequate follow-up for patients undergoing HCV infection treatment.

PEG 2a or 2b combined with ribavirin, the current standard care procedure, is effective in producing SVR in about half of the patients with chronic HCV infection. Optimizing the use of these antiviral agents, and the overall management of HCV infection, is essential to ensure that the best possible patient outcomes are achieved while long-term health care costs are minimized.

We need to be sure that the best care to patients with the most efficient use of health care resources is being provided. The 12-week stop rule is one specific measure that can minimize costs for patients who do not achieve EVR. Specialist pharmacies can extend access of patients to clinician services to help ensure adherence and intended outcomes of therapy. Methods to increase treatment effectiveness and potentially reduce HCV-related costs are necessary in Brazil.

Source of financial support: C.R.B. received a scholarship of Programa de Doutorado no País com Estágio no Exterior (PDEE) (Program of Development of Abroad Studies), and M.R.F. received a scholarship of postdoctoral studies. Both scholarships are funded by Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) (Brazilian Federal Agency for Support and Evaluation of Graduate Education). U.S. was supported in part by the ONCOTYROL Center for Personalized Cancer Medicine (K1-COMET Center), funded by the Austrian government.

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