

## Demographic and Anthropometrical Analysis and Genotype Distribution of Chronic Hepatitis C Patients Treated in Public and Private Reference Centers in Brazil

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Hepatitis C virus (HCV) infection is a serious public health problem, since 80% to 85% of HCV carriers develop a persistent infection that can progress into liver cirrhosis and hepatocarcinoma. Considering that the response of hepatitis C patients to combination therapy with interferon and ribavirin depends on HCV characteristics as well as on host features, we made a retrospective analysis of demographic and anthropometrical data and HCV genotype distribution of chronic hepatitis C patients treated in public and private reference centers in Brazil. The medical records of 4,996 patients were reviewed, 81% from public and 19% from private institutions. Patients' median age was 46 years, and there was a higher prevalence of male (62%) and white patients (80%). The analysis of HCV-infecting strains showed a predominance of genotype 1 (64%) over genotypes 2 and 3. The patients' mean weight was 70.6 kg, and 65% of the patients weighed less than 77kg. Overweight and obesity were observed in 37.8% and 13.6% of the patients, respectively. Since a body weight of 75 kg or less has been considered an independent factor that significantly increases the odds of achieving a sustained virological response, the Brazilian population seems to have a more favorable body weight profile to achieve a sustained response than the American and European populations. The finding that 65% of chronic hepatitis C patients have a body weight of 77 kg or less may have a positive pharmaco-economic impact on the treatment of genotype 1 HCV patients with weight-based doses of peginterferon.

**Key Words:** HCV, chronic hepatitis C, genotype, body weight, Brazil.

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Hepatitis C virus (HCV) was identified in 1989 [1]; it is responsible for about 90% of the so-called non-A non-B hepatitis. It is a RNA virus of the *Flaviviridae* (Flavivirus) family and *Hepacivirus* gender [2] that is primarily transmitted through infected blood [3].

HCV infection affects about 170 million people worldwide and is currently one of the major public health problems in Brazil and in the world [4]. According to

the Brazilian Hepatology Society, local epidemiological information is still incipient. Brazilian studies on this subject have been predominantly aimed at risk groups (drug addicts [5], patients undergoing hemodialysis [6] and blood donors [7-12]). So far, only a few investigators have addressed the prevalence of hepatitis C in the general population [13,14].

Focaccia et al. [13] made a populational, randomized and stratified study, and reported a prevalence of 1.42% of HCV carriers in the city of São Paulo, with rates increasing with age, reaching over 3.5% in individuals aged 30 years and over. In spite of HCV's low infectivity and slow replication rate, 80% to 85% of the patients will develop a persistent, asymptomatic (or oligosymptomatic) infection that may progress into liver cirrhosis in approximately 20% of the patients and into hepatocellular carcinoma in part of these cases [15,16].

Considering that the response of HCV patients to combination therapy with interferon and ribavirin depends on intrinsic HCV characteristics, such as genotype, as well as on host features such as sex, age, the degree of liver fibrosis [17] and body weight [18], we made a retrospective analysis of demographic and anthropometrical data and of HCV genotype distribution of chronic hepatitis C patients treated in public and private reference centers in Brazil.

## Material and Methods

A retrospective analysis was made of the medical records of HCV carriers older than 14 years followed up in 11 reference public institutions and four specialized private hospitals. Medical records of HCV patients treated within the two years preceding the study were sequentially included; 74% of the hepatitis C diagnoses were made after 1998. One or more health professionals designated by the principal investigator reviewed the medical records and transferred selected data into a "Data Collection Form".

The following data were collected: number of the medical record, patient's initials, age, sex, color, weight, height, HCV genotype and origin (geographic area,

private *versus* public institution) and entered in a computerized database that generated a report with descriptive statistics for all variables. After data collection, a second review was performed for a sample of 10% of the records by comparatively checking the information in the data collection forms and the respective source documents for quality assurance of the collection process. The  $\chi^2$  test was used for statistical analysis and significant differences were considered when  $p < 0.05$ .

## Results

### *Demographic data*

The medical records of 4,996 patients were reviewed, and 4,041 (81%) were from public and 955 (19%) from private institutions. Most data were collected in the southeast region of the country (69%), 27% in the south region and 4% in the northeast region. The patients were 15 to 98 years old, with a median age of 46 years, 50 years for females (16 - 87 years) and 44 years for males (15 - 98 years). Only 0.5% of the patients were 14 to 19 years old, 27.5% were 20 to 39 years old, 58% were 40 to 59 years old and 14% were 60 years or older. Sixty two percent were males and 38% were females. Eighty percent of the patients were white (Table 1).

### *HCV genotype*

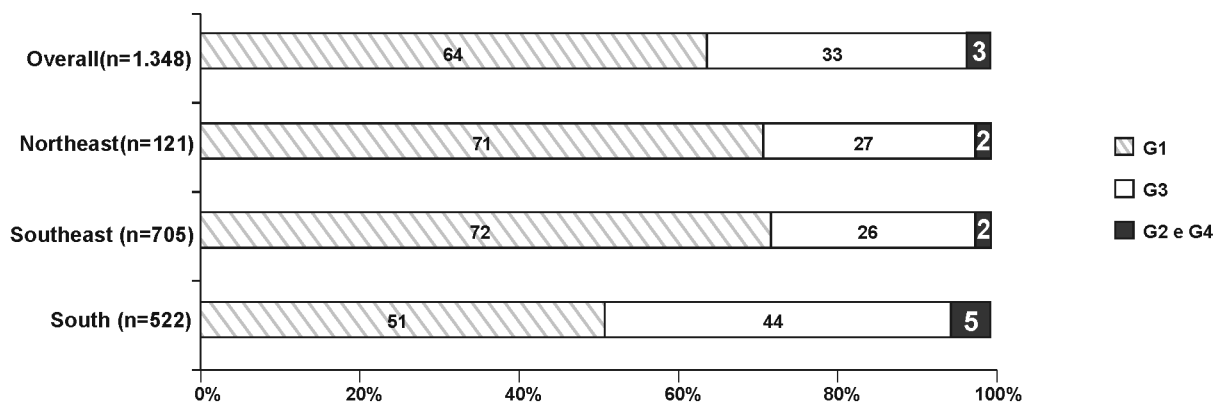
Information on the HCV genotype was available for only 27% of the medical records. The following distribution was observed: 64% for genotype 1, 3% for genotype 2 and 33% for genotype 3. The highest prevalence of genotype 3 was observed in the south region (Figure 1).

### *Anthropometrical data*

Information on patients' weight was available for 72% of the medical records. The patients mean weight was 70.6 kg, and it was significantly higher in males

**Table 1.** Demographic data of 4,996 Brazilian chronic hepatitis C patients

Characteristics	Values
<b>Gender</b>	
Male	61.5 %
Female	37.8 %
<b>Color</b>	
White	80%
Nonwhite	20%
<b>Age (Median, Range)</b>	
	46 yrs (15 – 98 yrs)
Female	50 yrs (16 – 87 yrs)
Male	44 yrs (15 – 98 yrs)
<b>Age distribution</b>	
14 - 19 yrs	0.5 %
20 - 39 yrs	27.5 %
40 - 59 yrs	58.0 %
> 60 yrs	14.0 %

**Figure 1.** Genotype distribution of hepatitis C virus in the three Brazilian geographic regions.

than in females (76.7 kg *versus* 64.9 kg, respectively) ( $p < 0.0001$ ). Most patients (65%) weighed less than 77 kg (Figure 2). No significant differences were observed between weight distributions among the three regions of the country (Figure 3) or between patients followed in public and private institutions (Figure 4).

Height data was available for 30.7% of the medical records, making it possible to calculate body mass index (BMI) for these patients. BMI was normal in 47.9% of the patients, whereas overweight and obesity were observed in 37.8% and 13.6% of the patients, respectively (Table 2).

## Discussion

It is well known that intrinsic HCV characteristics can influence the rates of sustained virological response (SVR) to interferon-based therapy; however, host features may also interfere with response to treatment [17,18]. Though retrospective studies might be inaccurate because of the way data are retrieved rather than how they are recorded, they are often the only source of information, especially in countries like Brazil, where prospective populational studies are not always feasible.

The median age of 46 years for the chronic hepatitis C patients in this study was very close to that reported in other Brazilian surveys by Bassit et al. (mean age of 47 years) [19] and by Medeiros-Filho et al. (mean age of 49.7 years). Similarly to the Medeiros-Filho's sample, most of the patients who were followed-up were 40 to 60 years old (60 and 58%, respectively) [20].

As reported by Bassit et al. [19], there was a higher prevalence of males (62%). Other publications have already shown this prevalence, reporting rates ranging from 64% to 72% [21-24]. This result probably reflects the characteristics of the blood donor population, constituted of presumably healthy adult males who seek medical assistance after being diagnosed in blood banks. In addition, it is known that drug abuse and sexual behaviors that predispose to sexually transmittable disease are more common among males [25].

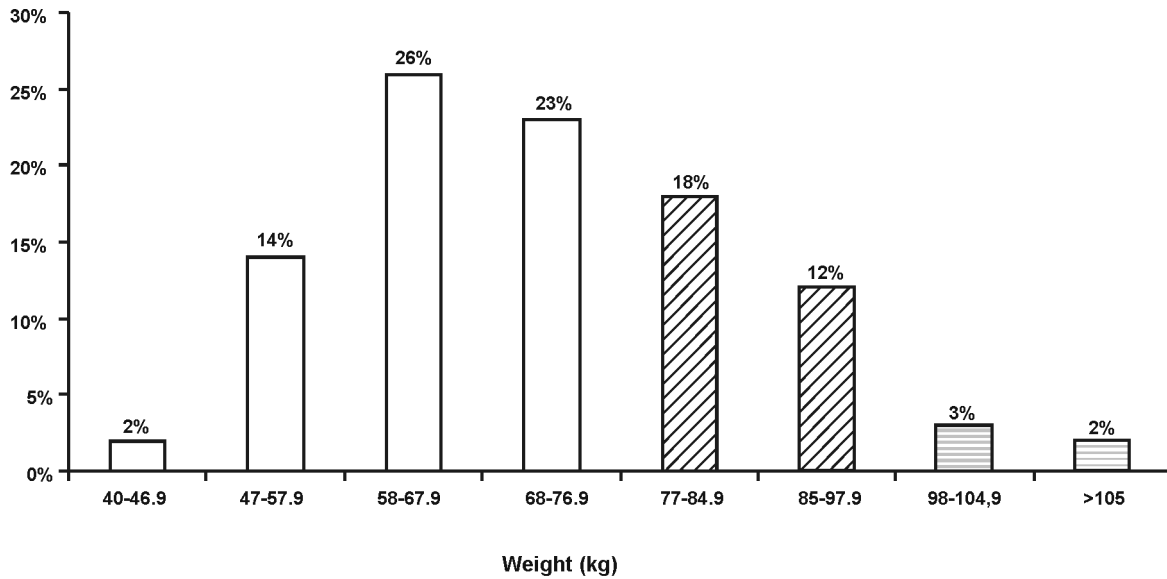
Although HCV genotype determines the duration of the combination therapy with interferon- $\alpha$  and ribavirin, HCV genotyping was carried out in only 27% of the patients under treatment. The distribution of HCV infecting strains was similar to that previously reported in other studies [19,26], with prevalence of genotype 1 (64%) over genotypes 2 and 3. The regional genotype distribution also confirmed the higher prevalence of genotype 3 in the south region reported by Campiotto et al. [26].

The scarcity of Brazilian anthropometrical data makes the interpretation of weight and BMI data in chronic HCV patients difficult. The percentage of obese and overweight patients was 51.4% in our sample, whereas a survey carried out in 1997 in southeast and northeast Brazil found an overweight and obesity prevalence of 38.5% [27]. The increased prevalence of overweight and obese patients observed in our study compared to that of 1997 might be due to regional differences; however, taking into consideration the influence of obesity associated with liver steatosis on the response to the combination therapy [28], further studies are required to clarify this issue.

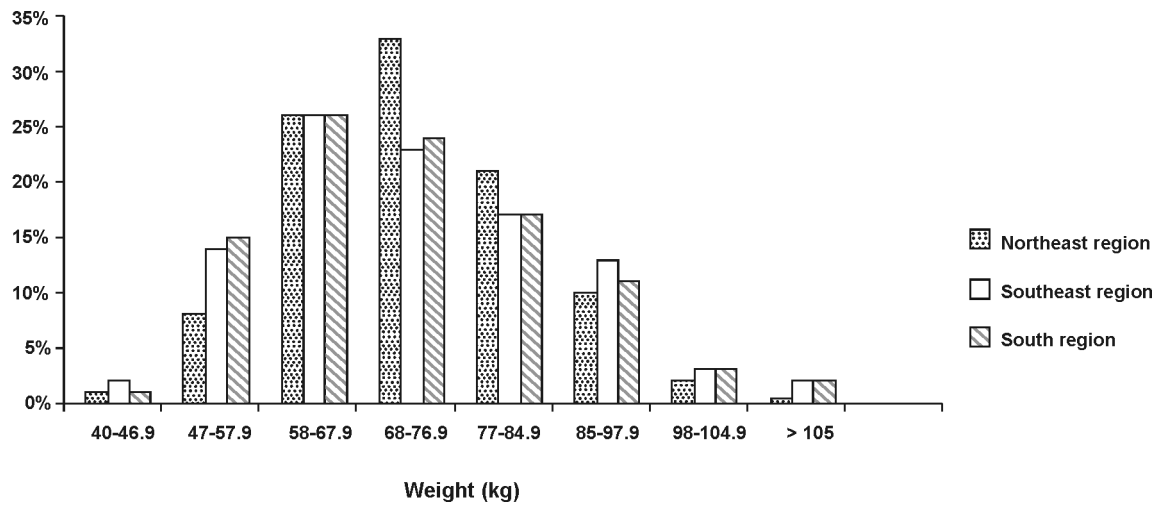
Analysis of the results of phase III clinical trials with interferon  $\alpha$ -2b have shown that SVR rates are greatly influenced by body weight, since smaller body weights were associated with higher sustained response rates [29]. The impact of body weight on SVR was also reported by a PEG IFN  $\alpha$ -2a monotherapy study [30] as well as by a PEG IFN  $\alpha$ -2a plus ribavirin study, where three factors were shown to independently and significantly increase the odds of achieving a SVR: a non-1 HCV genotype, age = 40 years and body weight = 75 kg [18].

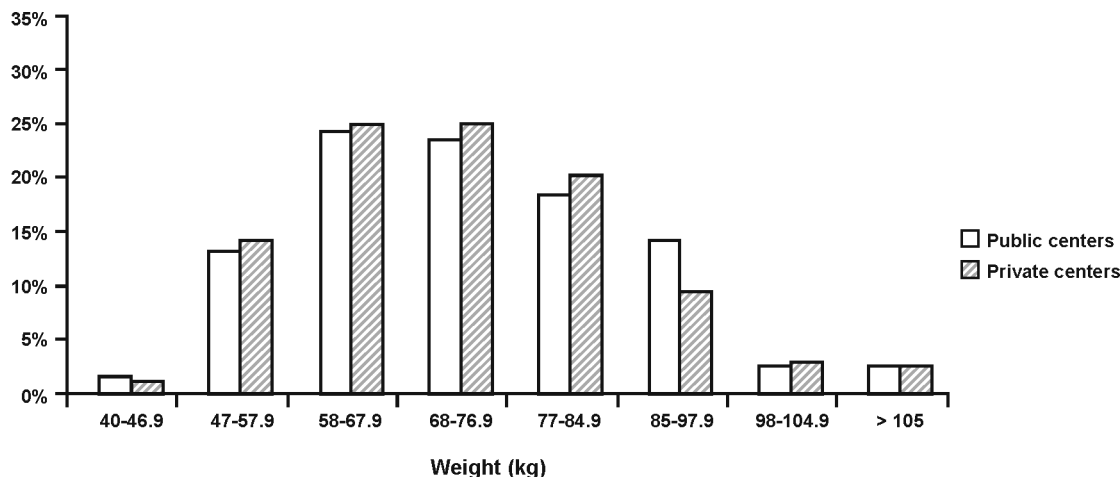
This is the first clinical study to evaluate the weight of chronic hepatitis C patients in Brazil. The mean weight of 70.6 kg observed in this survey suggests that the Brazilian population has a more favorable body weight profile to achieve a SVR than the American and European populations, whose mean weight has ranged from 73 kg to 82 kg [17,18,31,32] in previous studies with ribavirin and interferon or peginterferon. We also found that 65% of the chronic hepatitis C patients had a body weight of 77 kg or less. This finding may have

**Figure 2.** Distribution of chronic hepatitis C patients according to body weight.



**Figure 3.** Weight distribution of chronic hepatitis C patients according to geographic region.



**Figure 4.** Weight distribution of chronic hepatitis C patients according to reference center (public or private).**Table 2.** Body Mass Index of 1,533 Brazilian chronic hepatitis C patients

Body mass index	%
<25 (normal)	47.9
25-29.9 (overweight)	37.8
30-40 (obesity)	13.6
>40 (morbid obesity)	0.7

a positive pharmacoeconomic impact on the treatment of patients infected by genotype 1 with weight-based dosing of peginterferon. The inclusion of an economic perspective has become an increasingly accepted component to establish health care policies and planning [33], and knowing the population's characteristics may be useful when allocating scarce public health resources.

Therefore, it is essential that governmental strategies are developed to allow a better understanding of the HCV population and hence optimize resources in this important public health care problem.

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### References

1. Choo Q.L., Kuo G., Weiner A.J., et al. Isolation of a cDNA clone derived from a blood-borne non-A, non-B viral hepatitis genome. *Science* **1989**;244(4902):359-62.
2. Purcell R. The hepatitis C virus: overview. *Hepatology* **1997**;26(3 suppl 1):11S-4S.

3. Focaccia R., Baraldo D.C.M., Souza F.V. Hepatite C. Epidemiologia. In: Tratado de Hepatites virais. Focaccia R. São Paulo: Atheneu, **2003**: 221-9.
4. Report of a WHO Consultation organized in collaboration with the Viral Hepatitis Prevention Board, Antwerp, Belgium. Global surveillance and control of hepatitis C. *J Viral Hepat* **1999**;6:35-47.
5. Oliveira M.L., Bastos F.I., Telles P.R., et al. Prevalence and risk factors for HBV, and HDV infections among injecting drug users from Rio de Janeiro, Brazil. *Braz J Med Biol Res* **1999**;32(9):1007-14.
6. Yoshida C.F., Takahashi C., Gaspar A.M., et al. Hepatitis C virus in chronic hemodialysis patients with non-A non-B hepatitis. *Nefron* **1992**;60:150-3.
7. Parolin M.B., Russo A.A., de Almeida P.T., et al. Multicenter study on the prevalence of hepatitis C virus infection in blood donors in the city of Curitiba, Brazil. *Arq Gastroenterol* **1999**;36(3):117-21.
8. Patino-Sarcinelli F., Hyman J., Camacho L.A., et al. Prevalence and risk factors for hepatitis C antibodies in volunteer blood donors in Brazil. *Transfusion* **1994**;34(2):138-41.
9. Vanderborgth B.O., Reis A.M., Rouzere C.D., et al. Prevalence of anti-hepatitis C vírus in the blood donor population of Rio de Janeiro. *Vox Sang* **1993**;65(2):122-5.
10. Gonçalves Jr F.L., Boccato R.S.B.S., Pedro R.J. et al. Prevalências do HBsAg, do anti-HBc e do anti-HCV na população de candidatos a doadores de sangue do Hemocentro-Campinas. *Rev Inst Med Trop São Paulo* **1993**;35(1):45-51.
11. Gonçalves Jr F.L., Pedro R.J., Silva L.J., et al. Hepatites pós-transfusionais na cidade de Campinas, SP, Brasil. I – Incidência, agentes etiológicos e aspectos clínicos-epidemiológicos da hepatite por vírus C. *Rev Inst Med Trop São Paulo* **1993**;35(1):53-63.
12. Gonçalves Jr F.L., Pedro R.J., Silva L.J., et al. Hepatites pós-transfusionais na cidade de Campinas, SP, Brasil. II – Presença dos anticorpos anti-HBc e anti-HCV em candidatos a doadores de sangue e ocorrência de hepatites pós-transfusionais pelo vírus C nos receptores de sangue ou derivados. *Rev Inst Med Trop São Paulo* **1993**;35(1):63-71.
13. Focaccia R., Conceição O.J., Sette-Jr H., et al. Estimated prevalence of viral hepatitis on the general population of the municipality of Sao Paulo, measured by plasmatic markers through samples collected from stratified, randomized and residence-based population survey. *Braz J Infect Dis* **1998**;2:269-84.
14. Silva L., Parana R., Mota E., et al. Prevalence of hepatitis C virus in urban and rural populations of northeast Brazil – pilot study. *Arq Gastroenterol* **1995**;32(4):168-71.
15. Seef L.B., Buskell-Bales Z., Wright Z., et al. Long-term mortality after transfusion-associated non-A. non-B hepatitis. *New Eng J Med* **1992**;327:1906-11.
16. Takahashi M., Yamada G., Miyamoto R., et al. Natural course of chronic hepatitis C. *Am J Gastroenterol* **1993**;88:240-3.
17. Poynard T., Marcellin P., Lee S.S., et al. Randomised trial of interferon alpha2b plus ribavirin for 48 weeks or for 24 weeks *versus* interferon alpha 2b plus placebo for 48 weeks for treatment of chronic infection with hepatitis C virus. International Hepatitis Interventional Therapy Group (IHIT). *Lancet* **1998**;352(9138):1426-32.
18. Fried M.W., Shiffman M.L., Reddy K.R., et al. Peginterferon alfa-2a plus ribavirin for chronic hepatitis C virus infection. *N Engl J Med* **2002**;347(13):975-82.
19. Bassit L., Da Silva L.C., Ribeiro-dos-Santos G., et al. Chronic hepatitis C virus in Brazilian patients: association with genotypes, clinical parameters and response to long term alpha interferon therapy. *Rev Inst Med Trop Sao Paulo* **1999**;41(3):183-9.
20. Medeiros-Filho J.E., Gardia B.D., Nita S.K., et al. Aspectos epidemiológicos da infecção crônica pelo VHC no HC-FMUSP - São Paulo: Experiência de 628 casos. *GED - Gastroenterologia e Endoscopia Digestiva* **2001**;20(1):S40.
21. Merican I., Sherlock S., McIntyre N., et al. Clinical, biochemical and histological features in 102 patients with chronic hepatitis C virus infection. *Q J Med* **1993**;86:119-25.
22. Delladetsima J.K., Rassidakis G., Tassopoulos N.C., et al. Histopathology of chronic hepatitis C in relation to epidemiological factors. *J Hepatol* **1996**;24:27-32.
23. Van Thiel D.H., Friedlander L., Malloy P., et al. Gamma-glutamyl transpeptidase as a response predictor when using alfa-interferon to treat hepatitis C. *Hepatogastroenterology* **1995**;42(6):888-92.
24. Graf J., Toriyama K., Itakura H. A clinic-pathological study of 163 untreated cases of chronic hepatitis C. *Rev Soc Bras Med Trop* **1996**;29(1):21-5.
25. Conry-Cantilena C., VanRaden M., Gobble J., et al. Routes of infection, viremia, and liver disease in blood donors found to have hepatitis C virus infection. *N Engl J Med* **1996**;334(26):1691-6.
26. Campiotto S., Pinho J.R., Silva L.C., et al. Distribuição dos genótipos do vírus da hepatite C nas diferentes regiões do Brasil. Dados preliminares. *GED - Gastroenterologia e Endoscopia Digestiva* **1998**;17:S64.
27. Monteiro C.A., Conde W.L. A tendência secular da obesidade segundo estratos sociais: nordeste e sudeste do Brasil, 1975-1989-1997. *Arq Bras Endoc Metab* **1999**;43:186-94.
28. Poynard T., Ratziu V., McHutchison J., et al. Effect of treatment with peginterferon or interferon alfa-2b and ribavirin on steatosis in patients infected with hepatitis C. *Hepatology* **2003**;38(1):75-85.

29. McHutchison J.G., Poynard T., Salpetriere P., et al. Patient body weight and response to interferon alfa 2b monotherapy [abstract no. 998]. In: 52<sup>nd</sup> Annual Meeting of the American Association for the Study of Liver Diseases (AASLD); 2001 Nov 9-13; Dallas, Texas. *Hepatology* **2001**;34(4 Pt 2):407A.
30. Zeuzem S., Feinman V., Rasenack J., et al. Peginterferon alfa-2a in patients with chronic hepatitis C. *N Engl J Med* **2000**;343(23):1666-72.
31. McHutchison J.G., Gordon S.C., Schiff E.R., et al. Interferon alfa-2b alone or in combination with ribavirin as initial treatment for chronic hepatitis C. Hepatitis Interventional Therapy Group. *N Engl J Med* **1998**;339(21):1485-92.
32. Manns M.P., McHutchison J.G., Gordon S.C., et al. PegInterferon alfa-2b plus ribavirin compared with interferon alfa-2b plus ribavirin for initial treatment of chronic hepatitis C: a randomised trial. *Lancet* **2001**;358(9286):958-65.
33. Hutubessy R., Chisholm D., Edejer T.T. Generalized cost-effectiveness analysis for national-level priority –setting in the health sector. *Cost Eff Resour Alloc* **2003**;1:8.