



Universiteit  
Leiden  
The Netherlands

## **Hepatitis C and health-related quality of life among patients with hemophilia**

Posthouwer, D.; Plug, I.; Bom, J.G. van der; Fischer, K.; Rosendaal, F.R.; Mauser-Bunschoten, E.P.

### **Citation**

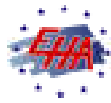
Posthouwer, D., Plug, I., Bom, J. G. van der, Fischer, K., Rosendaal, F. R., & Mauser-Bunschoten, E. P. (2005). Hepatitis C and health-related quality of life among patients with hemophilia. *Haematologica - The Hematology Journal*, 90(6), 846-850. Retrieved from <https://hdl.handle.net/1887/5041>

Version: Not Applicable (or Unknown)

License:

Downloaded from: <https://hdl.handle.net/1887/5041>

**Note:** To cite this publication please use the final published version (if applicable).



## Hepatitis C and health-related quality of life among patients with hemophilia

Dirk Posthouwer  
Iris Plug  
Johanna G. van der Bom  
Kathelijn Fischer  
Frits R. Rosendaal  
Eveline P. Mauser-Bunschoten

Hepatitis C has a negative effect on health-related quality of life (HRQoL). It is not clear whether hepatitis C affects HRQoL of patients with hemophilia. The objective of this study was to assess the effect of hepatitis C virus (HCV) infection on HRQoL in patients with hemophilia. A cross-sectional study was performed among all registered hemophilia patients in the Netherlands. HRQoL was determined by using the self-administered SF-36 questionnaire. Patients were eligible for the study if they completed the SF-36, had been treated with clotting factor products before 1992, and had reported their hepatitis C status. Data on the severity of hemophilia were obtained from the hemophilia treatment centers. The validity of the self-reported data on hepatitis C status was verified in a random sample of 92 (15%) patients; 92% reported their hepatitis C status correctly. Fifty-five percent (333/602) of the study population had a current HCV infection. All eight domains of the SF-36 were lower in patients with a current HCV infection than they were in patients who had never been infected with HCV. After adjustment for age, severity of hemophilia, human immunodeficiency virus (HIV) status, employment status, and joint limitations, hepatitis C infection was associated with a decrease of HRQoL on the domains of general health (difference 6.9 [95% confidence interval (C.I.) 2.7 to 11.2]) and vitality (3.8 [95% C.I. 0.1 to 7.7]). Hemophilia patients infected with HCV scored lower on the HRQoL domains of general health and vitality than hemophilia patients who had never been infected with HCV.

Key words: hemophilia, hepatitis C, HRQoL, survey

Haematologica 2005; 90:846-850

©2005 Ferrata Storti Foundation

From the Van Creveldkliniek, University Medical Center Utrecht, the Netherlands (DP, JGvdB, KF, EPM-B); Department of Clinical Epidemiology, Leiden University Medical Center, the Netherlands (IP, JGvdB, FRR); Wilhelmina Children's Hospital, University Medical Center Utrecht, the Netherlands (KF); Thrombosis and Hemostasis Research Center, Leiden University Medical Center, the Netherlands (FRR).

Correspondence:  
Dirk Posthouwer, Van Creveldkliniek, University Medical Center Utrecht Heidelberglaan 100, C.01.425, 3508 GA, Utrecht, The Netherlands. E-mail: D.Posthouwer@azu.nl

Hemophilia is an X-linked bleeding disorder caused by a partial or complete lack of clotting factor activity. Health-related quality of life (HRQoL) of these patients is lower than in the general population and is mainly dependent on severity of hemophilia, age, orthopedic status and comorbidities.<sup>1-4</sup> Hepatitis C is a major comorbid condition among patients with hemophilia who received non-virus-inactivated or insufficiently inactivated large-pool clotting factor concentrates or cryoprecipitate.<sup>5,6</sup> Hepatitis C infection itself has also been shown to be associated with a decrease in HRQoL, which may be explained by chronic liver disease and associated factors present in many infected individuals, such as intravenous drug use and low socioeconomic status.<sup>7-10</sup> Reports about the effect of hepatitis C virus (HCV) infection on HRQoL in patients with hemophilia are scarce. However, this information may be important with regard to the policy on initiating antiviral therapy. The majority of reports on HRQoL among patients with hepatitis C have focused on patients

selected for enrollment into treatment trials, from which patients with hemophilia are usually excluded.<sup>11,12</sup>

The aim of this study was to determine the effect of HCV infection on HRQoL among patients with hemophilia.

### Methods

Data for the present study were collected within the last survey of a series initiated by Veltkamp in 1972.<sup>13</sup> Since then nationwide surveys were performed in 1978, 1985, 1992 and in 2001.<sup>14-16</sup> These surveys were aimed at assessing the medical and social consequences of hemophilia in the Netherlands. In 2001, postal questionnaires were sent to all 1519 known hemophiliacs in the Netherlands, who were either registered at the Netherlands Hemophilia Patients' Society or at the hemophilia treatment centers, or known from previous surveys. In this last survey items on hepatitis C were added for the first time. The study was approved by the medical ethics committee of the Leiden University Medical Center.

The overall response rate to the ques-

tionnaire was 70% (1066/1519). Of those responding to the questionnaire, 771 patients had been treated with clotting factor products before 1992 and were at risk of HCV infection. Of those at risk, 638 patients reported their HCV test result and 602 completed the SF-36 questionnaire. The study population consisted of these 602 patients, treated with clotting products before 1992, with a reported HCV test result and a completed SF-36 questionnaire. Hemophilia type and severity of patients not responding to this questionnaire (n=453) were similar to those of the responding population (n=1066). The reasons for these patient's lack of participation in this study are not known. Socio-demographic and clinical data of patients at risk for HCV, who did not complete the SF-36 questionnaire (n=36) did not differ from those of the study population (n=602).

The questionnaire contained questions on type and severity of hemophilia, use of clotting products, health issues, complications and infections, education, and profession. The self-reported type and severity of hemophilia were verified with information from the treatment centers.

Hepatitis C status was defined as: never infected with HCV, infection in the past, or current infection. To assess the validity of the self-reported data on hepatitis C, a random sample of 92 patients (15%) was drawn from the two largest participating centers and these data were verified with information from the treating hematologists.

HRQoL was assessed by using the Dutch version of the SF-36 questionnaire.<sup>17-19</sup> This self-administered questionnaire contains 36 items assessing 8 domains of HRQoL: physical functioning, social functioning, role physical, role emotional, mental health, vitality, bodily pain and general health. Each HRQoL domain is given a score ranging from 0 to 100, with higher scores indicative of better quality of life. In addition, the physical and mental health component summaries were calculated using standard algorithms.<sup>20</sup> Table 1 explains the meaning of the different domains.

Joint status was assessed in terms of functional limitation of 16 joints; per joint, scores ranged from 0 (no limitation), 1 (some limitation without daily problems), 2 (some limitation with daily problems), to a maximum of 3 (severe limitation with complete loss of function). The total *joint limitation score* was calculated by adding up all joint scores resulting in a range from 0 to 48.

Employment and educational status were determined by asking patients about their work or school.

Descriptive statistics were calculated using means (95% confidence intervals, C.I.) and medians (range). Baseline characteristics and HRQoL scores of patients with a current HCV infection were com-

**Table 1.** Explanation of the domains of the SF-36.

Domain	Explanation
Physical functioning	Limitations in daily activities (e.g. walking, dressing)
Social functioning	Limitations in social activities (e.g. meeting friends)
Role physical	Difficulties with work or daily activities due to physical health problems
Role emotional	Difficulties with work or daily activities due to emotional problems
Mental health	Presence of depressive feelings or nervousness
Vitality	Loss of energy or presence of fatigue
Bodily pain	Presence of pain and its limitations due to pain
General health	Subjective evaluation of general health status

pared with those of patients who had never been infected using the T-test for continuous and normally distributed data, the Mann-Whitney U-test for continuous and skewed data and the  $\chi^2$ -test for ordinal or nominal data. A *p* value <0.05 was considered statistically significant.

To quantify the effects of HCV infection on HRQoL, linear regression models were used with physical and mental summary scores as dependent variables. In order to facilitate the interpretation of the effect of hepatitis C on HRQoL and to put this effect in perspective, we also determined the isolated effects of both age and severity of hemophilia on HRQoL. The effect of age was assessed in patients with mild hemophilia who had never been infected with HCV. The effect of disease severity was determined by comparing patients with mild versus severe hemophilia, among patients who had never been infected with HCV.

Multivariate linear regression models were used to adjust the association between HCV infection and HRQoL for age, severity of hemophilia, HIV status, joint limitation and employment/education status. Dummy variables for hepatitis C infection status and severity of hemophilia were created to differentiate among the groups in the regression analyses; the references were *never infected with HCV* and *mild hemophilia*, respectively. The regression coefficients represent the change in outcome (i.e. scores on domains of HRQoL), per unit increase of the determinant.

## Results

The study population consisted of 602 patients; 171 (28%) patients had never been infected with HCV, 98 (16%) had cleared HCV, and 333 (55%) patients had a

**Table 2.** Baseline characteristics of the study population according to HCV infection status.

	Never infected (n=171)	Infection in the past (n=98)	Current infection (n=333)	P value*
Age (years)	37 (11-87)	36 (13-87)	44 (13-83)	<0.001
Severe hemophilia	24%	55%	60%	<0.001
HIV positive	1%	2%	7%	<0.005
Joint limitation score (0-48)	2 (0-48)	4 (0-32)	7 (0-35)	<0.001
Employed/student	81%	80%	70%	<0.01

Values are medians (range) or percentages. \*Differences in baseline characteristics; patients who had never been infected compared with patients with a current HCV infection.

current HCV infection. In the verification sample, 92% (85/92) reported their hepatitis C status correctly; these proportions were 93%, 75% and 100% for patients with a current infection, an infection in the past, and patients who have never been infected, respectively. Table 2 presents the patients' characteristics according to hepatitis C status. Patients with a current HCV infection were older than those who had never been infected (44 years vs. 37 years). Furthermore, the proportions of patients with severe hemophilia and HIV, and total score of joint limitations were higher among patients currently infected with HCV than among patients who had never been infected. Patients with a current HCV infection had lower HRQoL scores on all domains and the physical component summary of the SF-36 questionnaire compared to those who had never been infected (Figure 1). Physical function, role physical and general health appeared to be the domains most affected by HCV infection. The mental component summary was similar in all groups.

In order to study potential confounders of the association between hepatitis C and HRQoL, we performed univariate analysis of several established determinants of HRQoL on the physical and mental component summaries of the SF-36 questionnaire (Table 3). Current HCV infection, increasing age, severe hemophilia, HIV, increasing joint limitation and unemployment were associated with lower scores on the physical component summary score. A lower score on the mental component summary was associated with increasing age, increasing joint limitation and unemployment. However, the effects of these determinants on the mental component summary were less pronounced than the effects on the physical component summary score.

**Table 3.** Crude effects of patients' characteristics on physical and mental component summary scores of the SF-36 (univariate regression).

	Physical component summary	Mental component summary
Current HCV	-8.4 (-10.5 to -6.3) <sup>§</sup>	-0.9 (-2.7 to 1.0)
Age (per 10 years)	-2.7 (-3.3 to -2.2) <sup>§</sup>	-0.8 (-1.3 to -0.3) <sup>†</sup>
Severe hemophilia	-8.0 (-10.0 to -5.9) <sup>§</sup>	1.2 (-0.6 to 3.1)
Joint limitation (per point)	-1.1 (-1.2 to -1.0) <sup>§</sup>	-0.2 (-0.3 to -0.1) <sup>§</sup>
HIV positive	-6.4 (-11.1 to -1.7) <sup>‡</sup>	2.4 (-1.5 to 6.3)
Employed/student*	11.3 (9.3 to 13.3) <sup>§</sup>	4.7 (2.8 to 6.5) <sup>§</sup>

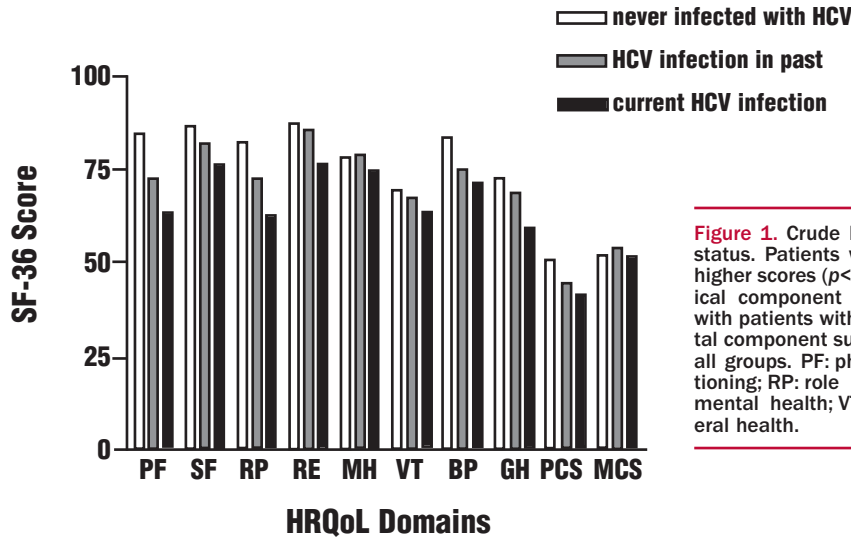
Values are regression coefficients (95% confidence interval). \*patients were classified as 'employed' when they worked full- or part-time; the young patients were classified as students as they attended school. <sup>†</sup>p value < 0.05. <sup>‡</sup>p-value < 0.001; <sup>§</sup>The presence of a current HCV infection resulted in a decrease of 8.4 points of the physical component summary.

A current HCV infection was associated with lower scores on all domains but the mental component summary score in the univariate analysis. After adjustment for age, severity of hemophilia, HIV status, joint limitations and employment/educational status, current HCV infection was only associated with a statistically significant decrease of the scores for general health (-6.9, 95% C.I. -11.2 to -2.7) and vitality (-3.8, 95% C.I. -7.7 to -0.1). In order to facilitate the interpretation of the effect of hepatitis C on the HRQoL domains of general health and vitality by putting this effect into perspective, we studied the isolated effects of age and severity of hemophilia on these domains (Table 5). For every 10 years the score of vitality decreased by 1.2 points (95% C.I. -1.1 to 3.5) and the score of general health by 1.7 points (95% C.I. -0.7 to 4.2) among patients with mild hemophilia without hepatitis C. We found no effect of disease severity on general health and vitality: scores were similar in patients with severe and mild hemophilia without hepatitis C.

## Discussion

In this nationwide study among 602 patients with hemophilia, patients with a current HCV infection scored lower than patients who had never been infected on all eight domains and the physical component summary of the SF-36 questionnaire. However, after adjustment for joint limitations, HIV status, age, employment/educational status, and severity of hemophilia, only the scores on the domains of general health and vitality of patients with HCV infection were affected.

To appreciate our findings some limitations of this study need to be discussed. Self-reported data may be



**Figure 1.** Crude HRQoL according to HCV infection status. Patients who had never been infected had higher scores ( $p < 0.05$ ) on all domains and the physical component summary score (PCS) compared with patients with a current HCV infection; the mental component summary score (MCS) was similar in all groups. PF: physical functioning; SF: social functioning; RP: role physical; RE: role emotional; MH: mental health; VT: vitality; BP: bodily pain; GH: general health.

**Table 4.** Crude and adjusted effects of current HCV infection on all domains of the SF-36.

HRQoL domain	$\beta$ current HCV (95% CI) unadjusted	$\beta$ current HCV (95% CI) adjusted*
Physical functioning	-22.1 (-27.5 to -16.8) <sup>†</sup>	-1.6 (-5.4 to 2.1)
Social functioning	-9.6 (-14.1 to -5.1) <sup>†</sup>	-3.2 (-7.7 to 1.2)
Role-physical	-19.5 (-27.0 to -12.0) <sup>†</sup>	-4.9 (-12.3 to 2.6)
Role-emotional	-11.1 (-17.6 to -4.7) <sup>†</sup>	-3.5 (-10.3 to 3.3)
Mental health	-4.0 (-7.2 to -0.8) <sup>†</sup>	-2.7 (-6.1 to 0.8)
Vitality	-6.5 (-10.1 to -2.8) <sup>†</sup>	-3.8 (-7.7 to -0.1) <sup>†</sup>
Bodily pain	-12.7 (-17.2 to -8.3) <sup>†</sup>	-3.5 (-7.8 to 0.9)
General health	-13.5 (-17.6 to -9.4) <sup>†</sup>	-6.9 (-11.2 to -2.7) <sup>†</sup>
Physical component score	-8.4 (-10.5 to -6.3) <sup>†</sup>	-1.6 (-3.4 to 0.1)
Mental component score	-0.9 (-2.7 to 1.0)	-1.5 (-3.6 to 0.6)

Values are regression coefficients (95% confidence interval); \*adjusted for age, severity of hemophilia, joint limitation, HIV and employment status; <sup>†</sup>p-value < 0.05; <sup>‡</sup>p-value < 0.001. Interpretation: the crude score on general health in patients with HCV infection was 13.5 points lower than that in patients who had never been infected with HCV. After adjustment the score for general health was 6.9 points lower in patients infected with HCV than in patients never infected with HCV.

**Table 5.** Effects of age and severe hemophilia on the domains of vitality and general health of the SF-36 (univariate regression).

	Vitality	General health
Age (per 10 years)	-1.2 (-3.5 to 1.1)	-1.7 (-4.2 to 0.7)
Severe hemophilia	-0.1 (-7.1 to 6.9)	0.6 (-6.6 to 7.8)

Values are regression coefficients (95% confidence interval). Regression coefficients for age were determined in patients with mild hemophilia and who had never been infected with HCV. Regression coefficients for severe hemophilia were determined in patients who had never been infected with HCV, with mild hemophilia as the reference variable.

unreliable. We therefore performed a validation study to check the accuracy of reported hepatitis C status, and found that these self-reported data were reliable. This confirms previous observations that most patients with hemophilia are well informed about their disease and its complications.<sup>15</sup>

Several studies have shown impaired HRQoL among patients with HCV infection compared with healthy, non-institutionalized members of the general population.<sup>7-10,21,22</sup> The effect of having HCV infection in the non-hemophilia population has been shown to lower the HRQoL score in the range from 10 to 30 points with the domains of role physical, general health, vitality and role emotional being most frequently affected. Hemophilia itself is also associated with a lower HRQoL compared with that found in the general population.<sup>14</sup> Increasing age, severe hemophilia, orthopedic status and HIV are reported to be predictors of a decreased HRQoL in patients with hemophilia.<sup>1-4</sup> The effect of hepatitis C on HRQoL in patients with hemophilia is unclear. One study reported a decreased HRQoL in hemophilia patients caused by hepatitis.<sup>2</sup> However, HRQoL was determined by the health utility index and hepatitis B and C were taken as one determinant in the analyses. This might be inappropriate as Foster *et al.* showed that hepatitis B and C have different effects on HRQoL.<sup>8</sup> After adjustment for confounding factors, we found that current HCV infection was associated with lower scores on the domains of general health and vitality only. These effects were relatively small but significantly stronger than the isolated effects of age and hemophilia severity. This indicates an important effect of hepatitis C on specific domains of HRQoL (vitality and general health) in patients with hemophilia.

Hepatitis C may reduce HRQoL through several mechanisms. Commonly reported symptoms of fatigue and tiredness may be partly responsible for this decrease. This is supported by two studies among HCV infected intravenous drug users showing lower scores of general health and vitality in patients aware of their hepatitis C status.<sup>23,24</sup> It was suggested that a diagnosis of hepatitis C raised concern and fear about current and future health status, resulting in a lower HRQoL. Fear about present and future health status is expected to predominantly affect the domain of general health. Indeed, in our study in which almost all patients were aware of their hepatitis C status, the domain of general health was affected most by the presence of HCV infection.

The majority of patients with hepatitis C in this study population have not been treated.<sup>25</sup> However, our findings demonstrate that specific domains of HRQoL are impaired among patients with hemophilia and hepatitis C. These results support the initiation of antiviral

treatment in this population, as successful treatment for hepatitis C has been proven to improve HRQoL and to be cost-effective as well.<sup>11</sup>

In conclusion, hemophilia patients infected with HCV had a lower HRQoL than hemophilia patients who were not infected with HCV. Current HCV infection was associated with lower scores on the domains of general health and vitality.

*DP: analysis and interpretation of data, drafting the article; IP: analysis and interpretation of data; JGvdB: conception and design of the study, analysis and interpretation of data; KF: analysis and interpretation of data; FRR, EPM-B: conception and design of the study, interpretation of data.*

*All authors revised this manuscript critically and approved it for publication. The authors declare that they have no potential conflicts of interest. The authors thank the patients who participated in the national questionnaire survey on hemophilia, conducted for the fifth time in 2001.*

*Manuscript received January 17, 2005. Accepted April 28, 2005.*

## References

- Molho P, Rolland N, Lebrun T, Dirat G, Courpied JP, Crougns T, et al. Epidemiological survey of the orthopaedic status of severe haemophilia A and B patients in France. The French Study Group. *Haemophilia* 2000;6:23-32.
- Barr RD, Saleh M, Furlong W, Horsman J, Sek J, Pai M, et al. Health status and health-related quality of life associated with hemophilia. *Am J Hematol* 2002; 71:152-60.
- Miners AH, Sabin CA, Tolley KH, Jenkinson C, Kind P, Lee CA. Assessing health-related quality-of-life in individuals with haemophilia. *Haemophilia* 1999; 5:378-85.
- Trippoli S, Vaiani M, Linari S, Longo G, Morfini M, Messori A. Multivariate analysis of factors influencing quality of life and utility in patients with haemophilia. *Haematologica* 2001;86: 722-8.
- Darby SC, Ewart DW, Giangrande PL, Spooner RJ, Rizza CR, Dusheiko GM, et al. Mortality from liver cancer and liver disease in haemophilic men and boys in UK given blood products contaminated with hepatitis C. UK Haemophilia Centre Directors' Organisation. *Lancet* 1997; 350:1425-31.
- Makris M, Preston FE, Triger DR, Underwood JC, Choo QL, Kuo G, et al. Hepatitis C antibody and chronic liver disease in haemophilia. *Lancet* 1990; 335:1117-9.
- Davis GL, Balart LA, Schiff ER, Lindsay K, Bodenheimer HC Jr, Perrillo RP, et al. Assessing health-related quality of life in chronic hepatitis C using the Sickness Impact Profile. *Clin Ther* 1994; 16:334-43.
- Foster GR, Goldin RD, Thomas HC. Chronic hepatitis C virus infection causes a significant reduction in quality of life in the absence of cirrhosis. *Hepatology* 1998; 27:209-12.
- Hussain KB, Fontana RJ, Moyer CA, Su GL, Sneed-Pee N, Lok AS. Comorbid illness is an important determinant of health-related quality of life in patients with chronic hepatitis C. *Am J Gastroenterol* 2001;96:2737-44.
- Bonkovsky HL, Woolley JM. Reduction of health-related quality of life in chronic hepatitis C and improvement with interferon therapy. The Consensus Interferon Study Group. *Hepatology* 1999;29:264-70.
- Siebert U, Sroczynski G, Rossol S, Wasm J, Ravens-Sieberer U, Kurth BM, et al. Cost effectiveness of peginterferon  $\alpha$ -2b plus ribavirin versus interferon  $\alpha$ -2b plus ribavirin for initial treatment of chronic hepatitis C. *Gut* 2003;52:425-32.
- Ware JE Jr, Bayliss MS, Mannocchia M, Davis GL. Health-related quality of life in chronic hepatitis C: impact of disease and treatment response. The Interventional Therapy Group. *Hepatology* 1999;30:550-5.
- Veltkamp JJ, Schrijver G, Willeumier W, van de Putte B, van Dijk H. Hemophilia in the Netherlands. Results of a survey on the medical, genetic and social situation of the Dutch hemophiliacs. *Acta Med Scand Suppl* 1974; 572: 3-24.
- Rosendaal FR, Varekamp I, Smit C, Brocker-Vriends AH, van Dijk H, Vandenbroucke JP, et al. Mortality and causes of death in Dutch haemophiliacs, 1973-86. *Br J Haematol* 1989;71:71-6.
- Plug I, Van Der Bom JG, Peters M, Mauser-Bunschoten EP, Goede-Bolder A, Heijnen L, et al. Thirty years of hemophilia treatment in the Netherlands, 1972-2001. *Blood* 2004; 104: 3494-500.
- Triemstra M, Rosendaal FR, Smit C, Van der Ploeg HM, Briet E. Mortality in patients with hemophilia. Changes in a Dutch population from 1986 to 1992 and 1973 to 1986. *Ann Intern Med* 1995;123:823-7.
- Hays RD, Morales LS. The RAND-36 measure of health-related quality of life. *Ann Med* 2001;33:350-7.
- van der Zee KI, Sanderma R. Het meten van de algemene gezondheidstoestand met de RAND-36: een handleiding. Groningen, the Netherlands: Noordelijk Centrum voor Gezondheidsvraagstukken. 1993.
- Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care* 1992;30:473-83.
- Ware JE Jr, Kosinski M, Keller SD. SF-36 Physical and Mental Health Summary Scales: A Users Manual. Nosto, MA. The Health Institute, New England Medical Center. 1994.
- Cordoba J, Flavia M, Jacas C, Saulea S, Esteban JI, Vargas V, et al. Quality of life and cognitive function in hepatitis C at different stages of liver disease. *J Hepatol* 2003;39:231-8.
- Gallegos-Orozco JF, Fuentes AP, Gerardo AJ, Perez-Pruna C, Hinojosa-Becerril C, Sixtos-Alonso MS, et al. Health-related quality of life and depression in patients with chronic hepatitis C. *Arch Med Res* 2003;34: 124-9.
- Dalgard O, Egeland A, Skaug K, Viliimas K, Steen T. Health-related quality of life in active injecting drug users with and without chronic hepatitis C virus infection. *Hepatology* 2004;39: 74-80.
- Rodger AJ, Jolley D, Thompson SC, Lanigan A, Crofts N. The impact of diagnosis of hepatitis C virus on quality of life. *Hepatology* 1999;30:1299-301.
- Posthouwer D, Plug I, van der Bom JG, Fischer K, Rosendaal FR, Mauser-Bunschoten EP. Hepatitis C infection among Dutch haemophilia patients: a nationwide cross-sectional study of prevalence and antiviral treatment. *Haemophilia* 2005;11:270-5.