Current and future health and economic impact of hepatitis C in Belgium

D. Vandijck[1,2], C. Moreno[3], P. Stärkel[4], P. Van Damme[5], H. Van Vlierberghe[6], S.J. Hindman[7], H. Razavi[7], W. Laleman[8]

(1) Ghent University, Dept. of Public Health, Ghent, Belgium ; (2) Hasselt University, Dept. of Health Economics & Patient Safety, Diepenbeek, Belgium ; (3) Erasme University Hospital, Université Libre de Bruxelles, Brussels, Belgium ; (4) Cliniques Universitaires Saint-Luc, Université Catholique de Louvain (UCL), Brussel, Belgium ; (5) Universiteit Antwerpen, Antwerpen, Belgium ; (6) Ghent University Hospital, Ghent, Belgium ; (7) Center for Disease Analysis (CDA), Louisville, Colorado, USA ; (8) University Hospitals Leuven, KU Leuven, Leuven, Belgium.

Abstract

Background and study aims : **Chronic hepatitis C virus (HCV) infection is a serious global health problem affecting 150 million individuals worldwide. Although infection rates are decreasing, an aging population with progressing disease is expected to result in increased burden of advanced stage disease with high associated costs. This analysis describes the current and projected future economic impact of HCV sequelae in Belgium.**

Methods : **A previously described and validated model was populated with Belgian inputs and calibrated to project the current and future health and economic burden of HCV. Monte Carlo and sensitivity analyses were run to quantify uncertainty. All estimates exclude the cost of antiviral therapy.**

Results : **Costs associated with HCV were projected to peak in 2026 at €126M (€30M-€257M), while decompensated cirrhosis and hepatocellular carcinoma costs were projected to increase until 2031 and 2034. The projected 2014-2030 cumulative cost of HCV under current conditions was €1,850M. Scenarios to reduce the burden of HCV could result in €70M-€400M in cumulative cost savings. Starting treatment (1,000 patients) in 2015 could result in €150M cost savings. The lifetime cost of HCV increases with life expectancy, with highest future costs projected among young females with early stage disease.**

Conclusions : **The economic burden of HCV and advanced stage disease were projected to further increase. Cost reductions are possible with timely interventions aimed at minimizing the health burden of advanced stage disease.** (Acta gastroenterol. belg., **2014**, 77, **285-290**).

Background

Chronic hepatitis c virus (HCV) infection is a serious global health problem that has been called a viral time bomb by the WHO due to its substantial prevalence, long term and unpredictable disease progression, aging population and low diagnosis and treatment rates (1-3). The current standard of care is successful in curing only 40-50% of patients (4), however new innovative and highly effective antiviral therapies have recently entered the market. These direct acting antivirals (DAAs) are projected to reach cure rates of 90-95% within the next 2-5 years.

Excluding costs associated with antiviral therapy, the economic burden of HCV is high due to the management of disease sequelae which present 20-30 years after infection (5). In Belgium, peak HCV prevalence was reached in 2003, suggesting that advanced stage disease will continue to increase until 2023-2033 (1). To compound the problem, due to significant limitations (including complex regimens and the cost of treatment), many diagnosed patients are currently left untreated or undertreated (6) and the latter are at high risk of developing severe complications requiring further (highly expensive) treatment interventions and procedures (7,8).

This analysis aims to describe the current and projected future costs associated with HCV sequelae in Belgium and to explore the economic impact of disease burden reduction strategies.

Methods

A previously described Microsoft Excel® (Redmond, WA) based model (1,5) was populated with Belgian data based on literature review, expert opinions and government reports, and HCV-disease progression and cost burden were modeled towards 2030. Monte Carlo simulation and bootstrap analysis were performed using Crystal Ball®, an Excel® add-in by Oracle®, to generate 95% uncertainty intervals (UI). The model was calibrated using the Excel® optimization add-in Solver®. Scenarios aimed at reducing the disease burden of HCV were developed and will be presented separately. A summary of the scenario assumptions is provided in Figure 1. The cost and cost savings associated with the modeled scenarios will be presented here. The future lifetime cost of chronic HCV was modeled by introducing 100 incident cases in 2014 and following the disease progression and cost over time. The individual cost was calculated by summing annual cost by disease sequelae from 2014-2100, and dividing by 100. Lifetime cost was modeled by age, gender and disease stage – Metavir fibrosis stages 0-3, cirrhosis, decompensated cirrhosis, HCC and liver transplant – but will be primarily summarized for a 30-34 year old, male patient.

Generally, costs were obtained from a 2012 analysis of HCV cost data in Belgium (8) except in the instance of liver transplant costs (Personal communication of Wim Laleman) and post-transplant costs (9). Costs were adjusted for the percent of the population estimated to be

Correspondence to : Dominique Vandijck, Hasselt University, Faculty of Business Economics, Dept. of Patient Safety & Health Economics, Agoralaan, building D, room B50, 3590 Diepenbeek, Belgium.
E-mail : dominique.vandijck@uhasselt.be

Submission date : 21/05/2014
Acceptance date : 22/05/2014

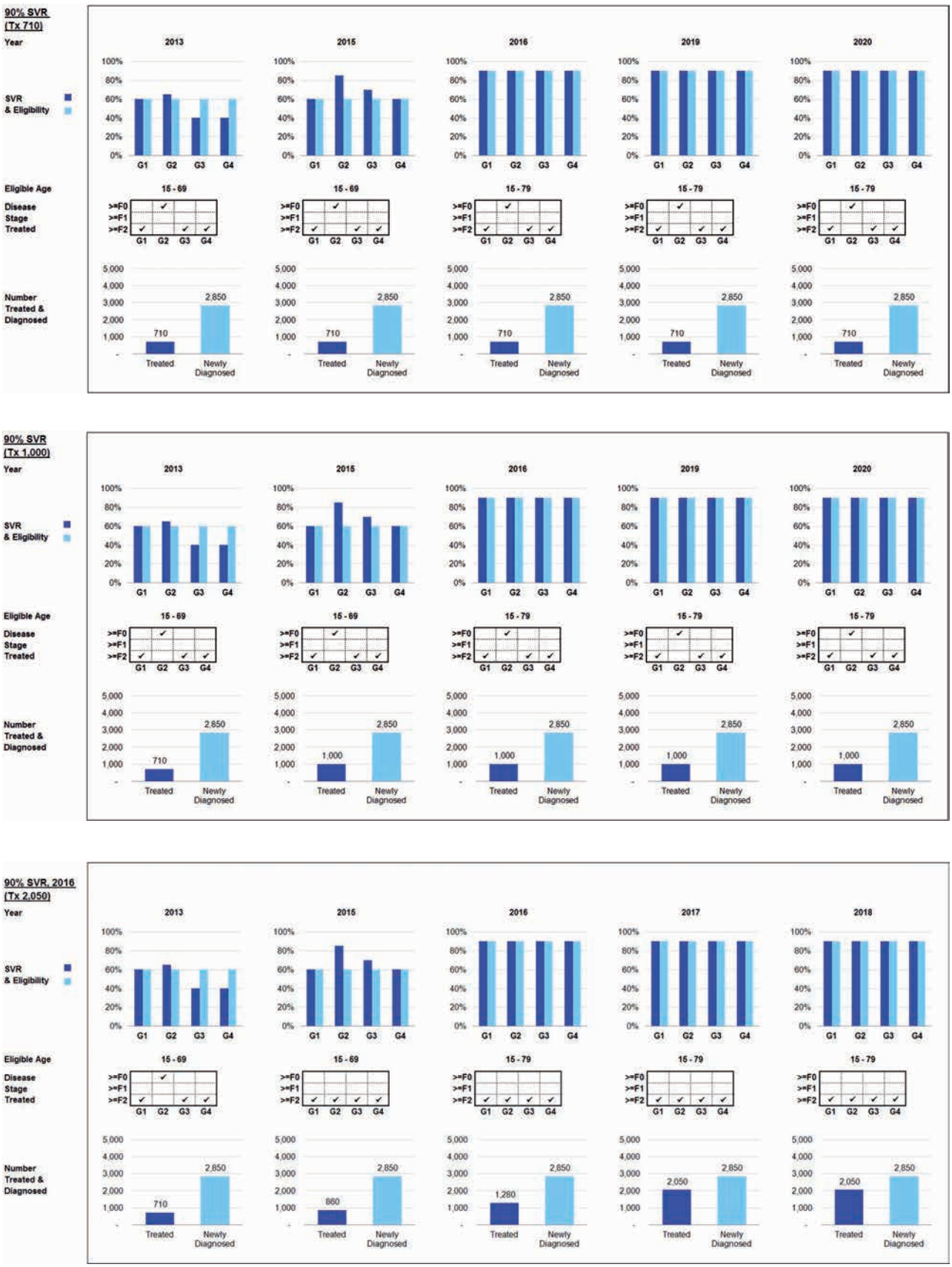

Fig. 1. — Scenario Inputs

diagnosed and were inflated to 2011 using medical CPI data from Statistics Belgium (10). Adjusting for diagnosis was particularly important for fibrosis costs, because only 20-25% of early stage cases are symptomatic (11), suggesting that 75-80% of patients are not incurring costs associated with their disease. Historical healthcare costs associated with HCV related disease sequelae were modeled without consideration for antiviral treatment cost. Additionally, future inflation was set at 1.

Cost Inputs

A 2012 analysis of HCV cost data presents costs by disease stage broken down by diagnosis, three years of follow up and cost of therapy (8). Standard deviation, obtained through bootstrapping, was published alongside each estimate (8). For the purposes of this model, it was important to have cost data presented annually and without therapy cost for fibrotic and cirrhotic stage patients. To achieve this transformation, Crystal Ball® was used to generate a new standard deviation. The article cites a non-normal distribution of costs ; however, the specific distribution used was not disclosed (8). In the absence of more complete information, a normal distribution was assumed to generate standard deviations for use in the model. To prevent the model from projecting negative costs, the distribution was bounded on the low end at 20% of fibrosis and cirrhosis base estimates, and 80% of decompensated cirrhosis and HCC estimates. Cost inputs, inflated to 2011, are presented in Table 1.

In 2011, the average cost of a liver transplant in Belgium was €99,998 (Range : €71,566-€113,965) (Personal communication of Wim Laleman) (12). The annual cost of a year of post-transplant follow up was obtained through an economic evaluation of HBV, in the absence of HBV antiviral cost (9). For HBV patients without antivirals, the 2006 average cost per patient was €7,047 and the average cost of a year of non HBV-related follow-up was €7,879 (9). These costs were inflated to 2011 and averaged to generate the base cost per patient for a year of post-transplant follow up.

Results

Although the HCV population in Belgium peaked in 2003, the cost associated with chronic HCV will increase until 2026, when peak costs were projected to reach €126M (95% UI : €30M-€257M) (Fig. 2). Costs associated with decompensated cirrhosis and HCC were projected to increase until 2031 and 2034 respectively, when they peaked at €14M and €8M (Fig. 3). Although costs were projected to decrease after 2026, by 2030 annual costs were estimated to be €119M (95% UI : €29M-€237M), a 49% increase from the 2014 annual cost of €80M (95% UI : €22M-€181M).

Lifetime cost analysis indicates that future costs associated with HCV are highest among individuals with longer life expectancy. This includes females, younger individuals and individuals with early stage disease or a recent liver transplant. Future costs associated with HCC are low as a result of increased HCC-associated mortality. For instance, in Belgium, a 30-34 year old male presenting with fibrosis is projected to incur €93,120 (95% UI : €36,800-€185,310) in HCV-related costs over a lifetime (Table 2, Fig. 4). By comparison, the same patient presenting with HCC would be expected to incur €34,680 (95% UI : €38,220-€94,970) in future costs.

Under today's standard of care (treat 710 patients annually with 40-65% SVR) the cumulative cost of HCV, excluding treatment cost, will be approximately €1,850 million between 2014 and 2030 (Fig. 5). A scenario with cure rates of 90% was expected to reduce cumulative costs associated with HCV disease sequelae by €70M. A scenario modeling the start of treatment beginning in 2015 (1,000 patients treated annually with 60-85% SVR), was expected to reduce cumulative costs associated with HCV disease sequelae by €150M. A scenario to simultaneously increase cure rates and treatment rates (2,050 patients treated annually with 90% SVR) could result in €400M in cumulative cost savings, if all oral therapies are available to the market by 2016. Delaying access to therapies by 2-years will reduce the economic impact of this scenario by €90M.

Table 1. — **2011 Model Estimated Costs**

2011 Model Estimates	Base Cost per Pt per Year	Standard Deviation/Low	High
Mild Fibrosis (F0 to F2)*	€ 1,919	€ 2,317	
Moderate Fibrosis (F3)*	€ 1,690	€ 2,337	
Compensated Cirrhosis (F4)*	€ 2,276	€ 1,873	
Decompensated Cirrhosis	€ 10,223	€ 12,128	
Hepatocellular Carcinoma	€ 12,362	€ 9,983	
Liver Transplant	€ 99,998	€ 71,566	€ 113,965
Liver Transplant - Subseq. Yrs	€ 8,564	€ 8,087	€ 9,041

*Indicates inputs that are modeled with annual adjustments for diagnosis rate

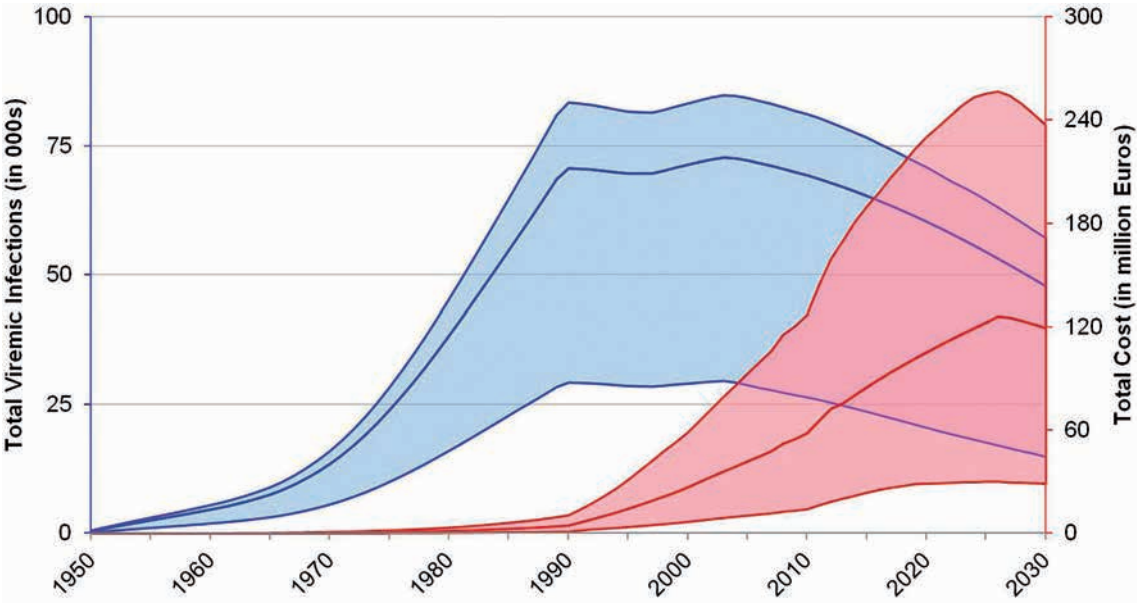

Fig. 2. — Total prevalence and cost, with 95% uncertainty interval, 1950-2030

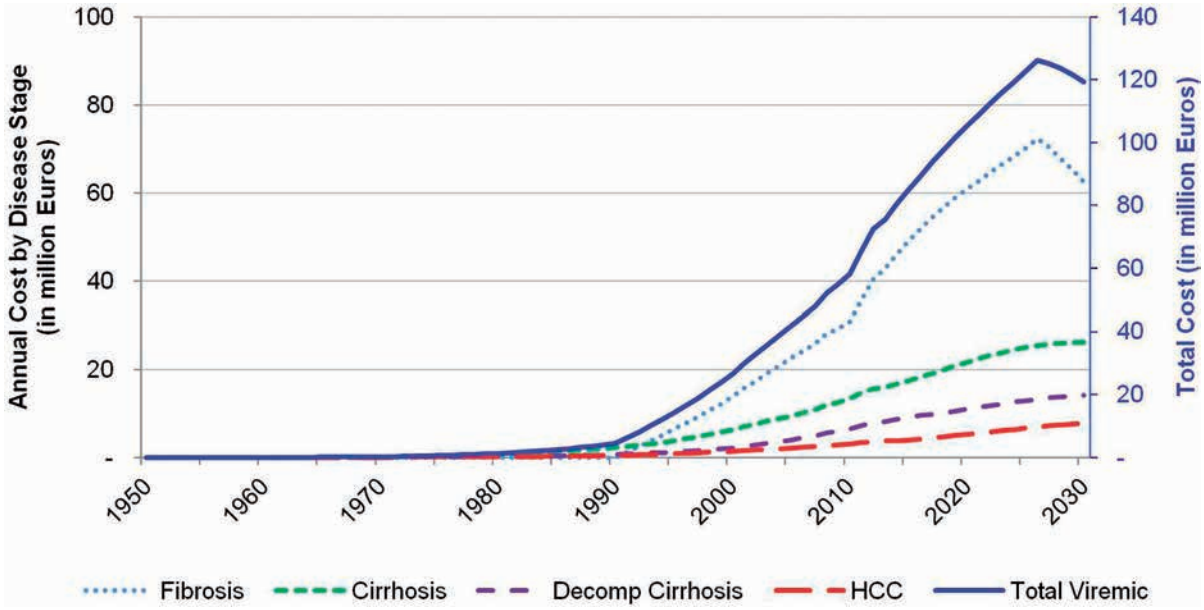

Fig. 3. — Projected HCV sequelae cost : Belgium, 1950-2030

Discussion

The cost of HCV and HCV-related disease sequelae in Belgium was projected to increase for another 12-20 years, despite reaching peak prevalence in 2003. By 2030, annual costs were projected to be 49% higher than in 2014. This is consistent with a recent analysis from the US, which suggested a three decade lag between peak prevalence and peak healthcare cost (5).

Sensitivity analysis identified the cost of mild fibrosis (8) as the key driver for variability in 2014 cost, accounting for 58% of the variance. The range surrounding the prevalence estimate (12,13) accounted for an additional 20% of variance.

This analysis exploring the costs associated with HCV (including cost of complications and excluding cost of antivirals) showed high lifetime costs associated with HCV. For a hypothetical male patient 30-34 years of age with fibrosis, cirrhosis or decompensated cirrhosis the estimated future cost was €93,000. This finding was surprising as a similar analysis in Canada, showed costs increasing incrementally from fibrosis to decompensated cirrhosis (14). This discrepancy is most likely driven by the high cost of fibrosis in Belgium. A key insight,

Table 2. — **Estimated future lifetime cost of a 30-34 year old male**

Future Lifetime Cost (in Euros) for a 30-34 year old Male Patient	Base	Low	High
Chronic HCV (F0)	93,120	36,800	185,312
F1	94,289	43,539	202,033
F2	94,990	50,979	179,961
F3	94,025	53,596	188,844
Compensated Cirrhosis	93,834	57,621	186,771
Decompensated Cirrhosis	89,996	70,574	216,733
Hepatocellular Carcinoma	34,679	24,054	94,970
Liver Transplant	151,229	131,491	161,943

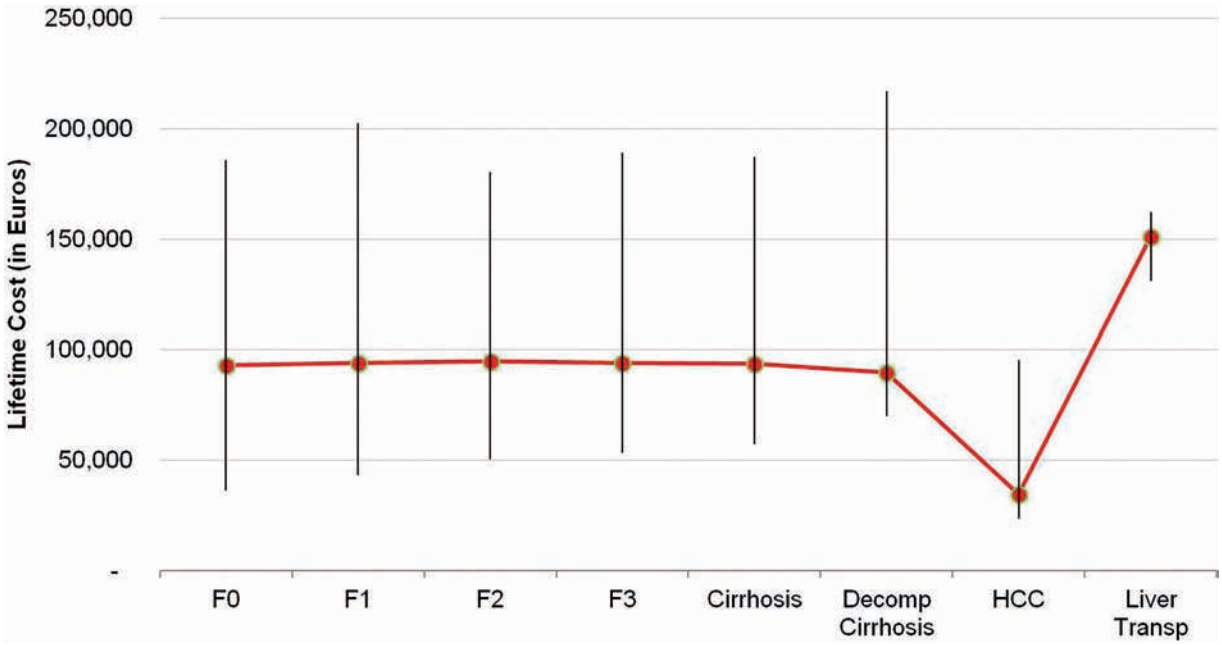

Fig. 4. — Estimated future lifetime cost of a 30-34 year old male, with 95% uncertainty interval, by disease stage

however, is the correlation between life expectancy and cost. Younger, early stage cases in Belgium are projected to incur higher costs over a lifetime than older, late stage cases primarily due to increased mortality of the latter group. This suggests that although treatment of late stage patients is necessary to improve quality of life and prevent mortality, there is substantial benefit to treating young patients before they progress to advanced and costly stage illness.

Healthcare cost savings associated with scenarios to reduce the burden of HCV in Belgium, have been presented here. Over the next 16 years, the costs associated with the current standard of care will be roughly €1,850M. The largest cost savings are associated with a scenario to treat nearly three times more patients with 90% SVR therapies. A two year delay in treatment access could result in a €90M loss in potential cost savings. Treating the same number of patients as today, with higher SVR therapies would result in €70M in cost savings,

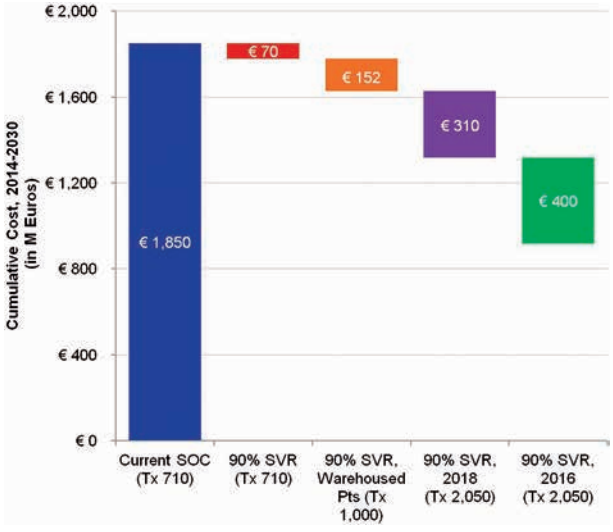

Fig. 5. — Cumulative cost of current therapy, with cost savings associated with disease control strategies 2014-2030.

and treating 1,000 patients annually would result in €150M in cost savings.

Limitations

There are a few notable limitations surrounding the model inputs and analysis. The study used for cost estimates was well conducted and reliable, however the distribution used to generate estimates of uncertainty was not stated. Thus, choosing the same distribution for the analyses presented here was not possible. To avoid negative cost projections, the distribution was bounded on the low end. The primary impact of this limitation is a very broad 95% uncertainty interval surrounding cost projections.

Additionally, this analysis assumes that the average cost of treatment for fibrotic and cirrhotic patients is dependent on the rate of diagnosis among these populations. For example, if 20% of fibrotics are diagnosed, this 20% is assumed to incur €1,919 in costs. Meanwhile, the remaining 80% of the population is assumed to incur €0 in costs. On average this equates to approximately €383 per case (diagnosed or undiagnosed). If, however, 100% of fibrotics are diagnosed, then the average cost per case would be €1,919. While this is a more accurate representation of costs associated with these disease stages, there may be variability in the true diagnosis rate in these populations.

Furthermore, this analysis excludes costs associated with antiviral treatment of HCV as well as future inflation to avoid making projections on future costs associated with treatment. Thus these estimates may be conservative projections. Additionally analysis does not take into account the indirect costs (sick days, lower productivity, etc.) associated with HCV and which are also assumed to be significant.

Despite decreasing HCV infection rates, the clinical and economic impact of chronic HCV infection is expected to grow in the coming decades as previously infected individuals progress to advanced stage disease. Currently, HCV is a leading cause of liver transplants worldwide, with high average costs and long waiting lists for transplants. Curing patients of HCV prior to progressing to advanced stage disease and so before needing a transplant would significantly reduce the burden on the healthcare system and patients alike. Thus, more effective treatment options and timely care are crucial for addressing the costs and public health impact of HCV.

References

1. RAZAVI H., WAKED I., SARRAZIN C. *et al*. The present and future disease burden of hepatitis C virus (HCV) infection with today's treatment paradigm. *J. Viral. Hepat*., 2014, **21** Suppl 1 : 34-59.
2. BRUGGMANN P., BERG T., OVREHUS A.L. *et al*. Historical epidemiology of hepatitis C virus (HCV) in selected countries. *J. Viral. Hepat*., 2014, **21** Suppl 1 : 5-33.
3. WEDEMEYER H., DUBERG A.S., BUTI M. *et al*. Strategies to manage hepatitis C virus (HCV) disease burden. *J. Viral. Hepat*., 2014, **21** Suppl 1 : 60-89.
4. MC HUTCHISON J.G., LAWITZ E.J., SHIFFMAN M.L. *et al*. Peginterferon alfa-2b or alfa-2a with ribavirin for treatment of hepatitis C infection. *N. Engl. J. Med*., 2009, **361** : 580-93.
5. RAZAVI H., ELKHOURY A.C., ELBASHA E. *et al*. Chronic hepatitis C virus (HCV) disease burden and cost in the United States. *Hepatology*, 2013, **57** : 2164-70.
6. ECONOMIST INTELLIGENCE UNIT. The silent pandemic : Tackling hepatitis C with policy innovation. Janssen Pharmaceutica NV, 2012.
7. LANG K., WEINER D.B. Immunotherapy for HCV infection : next steps. *Expert. Rev. Vaccines*, 2008, **7** : 915-23.
8. NEVENS F., COLLE I., MICHIELSEN P. *et al*. Resource use and cost of hepatitis C-related care. *Eur. J. Gastroenterol. Hepatol*., 2012, **24** : 1191-8.
9. SCHWIERZ C., THIRY N., VAN DE SANDE S. *et al*. Economic Evaluation of Antiviral Treatment of Chronic Hepatitis B - Part 2. Report (electronic). Brussels : Belgian Health Care Knowledge Centre (KCE), 2011 Jun 14. Report No. : 157A.
10. Statistics Belgium. Consumer Price Indices : Price Index Since 1920 and Health Index Since 1994.2013 [cited : May 6, 2013] Available from : URL : http://statbel.fgov.be/en/statistics/figures/economy/consumer_price_index/
11. FRETZ R., NEGRO F., BRUGGMANN P. *et al*. Hepatitis B and C in Switzerland-healthcare provider initiated testing for chronic hepatitis B and C infection. *Swiss Med. Wkly*., 2013, **143** : 0.
12. GERKENS S., MARTIN N., THIRY N., HULSTAERT F. [Hepatitis C : Screening and Prevention] HEPATITIS C : SCREENING EN PREVENTIE. *Belgian Health Care Knowledge Center (KCE)*, 2012.
13. QUOILIN S., HUTSE V., VANDENBERGHE H. *et al*. A population-based prevalence study of hepatitis A, B and C virus using oral fluid in Flanders, Belgium. *Eur. J. Epidemiol*., 2007, **22** : 195-202.
14. MYERS R.P., KRAJDEN M., BILODEAU M. *et al*. Burden of disease and cost of chronic hepatitis C infection in Canada. *Canadian Journal of Gastroenterology & Hepatology*, 2014, **28** : 243-50.