The Disease Burden of Hepatitis C in Belgium: An update of a realistic disease control strategy

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Abstract

Background: This manuscript serves as an update to position papers published in 2014 based on the available Belgian hepatitis C virus (HCV) epidemiological data.

Methods: Building on the current standard of care (2015: 900 ± F3 patients treated with 70-85% SVR), four new scenarios were developed to achieve the goals of near viral elimination and prevention of HCV associated morbidity and mortality by 2026 and 2031. Increases in treatment efficacy were assumed in 2016 (90% SVR) and 2017 (95% SVR).

Results: Scenario 1: Treating 6,670 patients annually by 2018 (≥ F0 beginning in 2017) and diagnosing 3,790 patients annually by 2020, a 90% reduction in viremic cases and advanced outcomes was observed by 2026.

Scenario 2: Treating 4,300 patients annually by 2018 (≥ F0 beginning in 2020) without increasing the number diagnosed, a 90% reduction in viremic cases and 85%-95% reduction in advanced outcomes was observed by 2031.

Scenario 3: Treating 5,000 ± F2 patients annually by 2018, and diagnosing 3,620 patients annually by 2020, a 90% reduction in advanced outcomes and 50% reduction in viremic cases was observed by 2026.

Scenario 4: Treating 3,100 ± F2 patients annually by 2018 without increasing the number diagnosed, a 90%-95% reduction in advanced outcomes and 55% reduction in viremic cases was observed by 2031.

Conclusions: Scenario 2 would provide the most favorable balance of outcomes (90% reduction in viremic prevalence and advanced outcomes) and realistic requirements for implementation (gradual increase in treatment, delayed incorporation of patients with no/mild fibrosis). (Acta gastroenterol. belg., 2015, 78, 228-232)

Key words: HCV mortality, hepatocarcinoma, interferon free treatment costs, viral elimination.

Background

In 2014, the Belgian Working Group for HCV published a series of position papers based on the available hepatitis C virus (HCV) epidemiological data in Belgium as well as the impact of modeled scenarios on the anticipated disease and cost burden associated with untreated HCV through 2030 (1-4). This exercise was part of a larger effort to quantify the burden of HCV worldwide (5-10) and followed a standard methodology (10). Since completion of this analysis, however, the HCV landscape in Belgium has changed more rapidly than expected, and previously modeled scenarios have already become outdated.

Beginning on January 1, 2015, all oral treatment with Sofosbuvir and Simeprevir became available in Belgium (much earlier than initially modeled). Access to this treatment is currently limited to patients with advanced fibrosis (≥ F3). Today, nearly all ≥ F3 patients with genotype 1 (G1) or G4 are being treated with this interferon free regimen (sofosbuvir-simeprevir +/- ribavirin). Within the next year, an additional antiviral, daclatasvir, is anticipated to become available in Belgium, extending interferon-free treatment options to G3 patients with advanced fibrosis.

Given the expanding treatment landscape, an updated analysis was conducted to explore steps necessary to substantially reduce the burden of HCV, including scenarios to 1) achieve near-viral elimination (90% reduction of viremic cases) and 2) prevent HCV-associated morbidity and mortality (90% reduction of advanced outcomes, including hepatocellular carcinoma [HCC] and liver-related mortality). These outcomes have been assessed at two endpoints, 10 years (2026) and 15 years (2031), for a total of four scenarios.

Methods

A Microsoft Excel-based model was populated with Belgian data as previously described (2-4,10).

Modeled scenarios and baseline treatment assumptions

Current Standard of Care (SOC): Under the current SOC scenario, prior to 2015, 710 patients (11) were treated annually with Peg/IFN + RBV (sustained viral response [SVR] 40%-65%, based on genotype) (12,13). Treatment was provided for adults (≥ 18 years of age) of all fibrosis stages (≥ F0 for G2 and ≥ F2 for G1, G3 and G4). Approximately 40% of patients were contra-indicated for treatment or refused treatment altogether.

Beginning in 2015, an estimated 900 patients were treated annually with new therapies (SVR G1, G2& G4-85%; SVR G3-70%), with treatment restricted to ≥ F3 patients.

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Reducing HCV prevalence of advanced outcomes

Modeled scenarios: Beginning in 2016, new scenarios included an increase in SVR to 90% for all genotypes. The percent of patients contraindicated for, or refusing, treatment was reduced to 10% to reflect the increased tolerability of treatment regimens. In 2017, a final increase in SVR to 95% was modeled in all patients.

Assuming increased treatment efficacy as described above, four scenarios were developed to explore two primary outcomes with two primary endpoints:

Scenario 1: Near-viral elimination (90% reduction in viremic cases) in 10 years
Scenario 2: Near-viral elimination (90% reduction in viremic cases) in 15 years
Scenario 3: Morbidity and mortality prevention (90% reduction in advanced outcomes) in 10 years
Scenario 4: Morbidity and mortality prevention (90% reduction in advanced outcomes) in 15 years

Cost analysis: For the base case and all four scenarios, the cumulative cost of untreated HCV was calculated using the methodology (3) and inputs (14-16) previously described.

Residual risk of HCC analysis: The model does not consider the residual risk of HCC development among HCV cirrhotic patients who achieve SVR, so a secondary analysis was performed to estimate this burden. An HCC incidence rate of 1.02% was applied to the cirrhotic population with SVR, after accounting for background mortality (17).

Table 1. — Impact on viremic cases, HCC and liver related deaths in 10 and 15 years, by scenario, compared with the current SOC

<table>
<thead>
<tr>
<th></th>
<th>2015 Estimate</th>
<th>2026 Estimate</th>
<th>% reduction, compared with Current SOC 2026</th>
<th>2031 Estimate</th>
<th>% reduction, compared with Current SOC 2031</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Viremic Cases</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current SOC</td>
<td>67,200</td>
<td>53,000</td>
<td>–</td>
<td>46,300</td>
<td>–</td>
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<tr>
<td>Scenario 1</td>
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<td>5,100</td>
<td>90%</td>
<td>1,500</td>
<td>95%</td>
</tr>
<tr>
<td>Scenario 2</td>
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<td>23,700</td>
<td>55%</td>
<td>4,500</td>
<td>90%</td>
</tr>
<tr>
<td>Scenario 3</td>
<td>67,200</td>
<td>25,500</td>
<td>50%</td>
<td>19,700</td>
<td>55%</td>
</tr>
<tr>
<td>Scenario 4</td>
<td>67,200</td>
<td>34,300</td>
<td>35%</td>
<td>20,700</td>
<td>55%</td>
</tr>
<tr>
<td><strong>HCC</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current SOC</td>
<td>290</td>
<td>330</td>
<td>–</td>
<td>315</td>
<td>–</td>
</tr>
<tr>
<td>Scenario 1</td>
<td>290</td>
<td>25</td>
<td>90%</td>
<td>10</td>
<td>95%</td>
</tr>
<tr>
<td>Scenario 2</td>
<td>290</td>
<td>125</td>
<td>60%</td>
<td>25</td>
<td>95%</td>
</tr>
<tr>
<td>Scenario 3</td>
<td>290</td>
<td>30</td>
<td>90%</td>
<td>&lt;5</td>
<td>&gt;95%</td>
</tr>
<tr>
<td>Scenario 4</td>
<td>290</td>
<td>115</td>
<td>65%</td>
<td>15</td>
<td>95%</td>
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<tr>
<td><strong>Liver-related deaths</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Current SOC</td>
<td>415</td>
<td>480</td>
<td>–</td>
<td>480</td>
<td>–</td>
</tr>
<tr>
<td>Scenario 1</td>
<td>415</td>
<td>55</td>
<td>90%</td>
<td>5</td>
<td>&gt;95%</td>
</tr>
<tr>
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<td>60%</td>
<td>65</td>
<td>85%</td>
</tr>
<tr>
<td>Scenario 3</td>
<td>415</td>
<td>45</td>
<td>90%</td>
<td>5</td>
<td>&gt;95%</td>
</tr>
<tr>
<td>Scenario 4</td>
<td>415</td>
<td>175</td>
<td>65%</td>
<td>45</td>
<td>90%</td>
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</tbody>
</table>
Scenario 3: Morbidity and mortality prevention (90% reduction in advanced outcomes) in 10 years

In order to reduce advanced stage outcomes by nearly 90% in 10 years, the number of patients treated with higher SVR therapies would have to increase from 900 in 2015 to 5,000 in 2018, with a 10% increase in annual diagnosed patients (from 2,850 in 2015 to 3,620 in 2020). Beginning in 2017, treatment would be provided to ≥F2 patients. At this treatment level, the majority of ≥F2 patients would be treated by 2024, at which point annual treatment could be reduced to ~3,000 ≥F2 patients through 2026. This scenario would result in a 90% reduction in HCV-related HCC and liver-related deaths by 2026, and total HCV infections would be reduced by

Table 2. — The 10 year and 15 year cumulative cost of untreated HCV by scenario, compared with the current SOC

<table>
<thead>
<tr>
<th>Scenario</th>
<th>10 year (2016-2026)</th>
<th>15 year (2016-2031)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cumulative Cost</td>
<td>Cost Savings</td>
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<td>Current SOC</td>
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<td>Scenario 1</td>
<td>€ 606</td>
<td>€ 530</td>
</tr>
<tr>
<td>Scenario 2</td>
<td>€ 763</td>
<td>€ 373</td>
</tr>
<tr>
<td>Scenario 3</td>
<td>€ 775</td>
<td>€ 362</td>
</tr>
<tr>
<td>Scenario 4</td>
<td>€ 881</td>
<td>€ 255</td>
</tr>
</tbody>
</table>

Fig. 1. — Annual treated patients, viremic cases, HCC and liver related deaths, by scenario - Scenario 1) Near-viral elimination (90% reduction in viremic cases) in 10 years; Scenario 2) Near-viral elimination (90% reduction in viremic cases) in 15 years; Scenario 3) Morbidity and mortality prevention (90% reduction in advanced outcomes) in 10 years; Scenario 4) Morbidity and mortality prevention (90% reduction in advanced outcomes) in 15 years.

Scenario 2: Near-viral elimination (90% reduction in viremic cases) in 15 years

In order to achieve near-viral elimination in 15 years, the annual increase in treatment with higher SVR therapies would be less aggressive, from 900 in 2015 to 4,300 in 2018. As in the 10-year scenario, treatment restrictions would need to be modified over time, including treatment of ≥F2 patients beginning in 2016 and all patients (≥F0) beginning in 2020. This scenario would result in a 90% reduction in total HCV infections and an 85%-95% reduction in HCV-related HCC and liver-related deaths by 2031 (Fig. 1). The cumulative cost savings, compared with the current SOC, would be € 770 M (45%), over 15 years (Fig. 2b).

Fig. 2. — Table 2: The 10 year and 15 year cumulative cost of untreated HCV by scenario, compared with the current SOC.
Reducing HCV prevalence of advanced outcomes


and treated patients, and explored the impact of time delays on HCV-related outcomes. The current analysis expands on previous efforts by examining the steps necessary to achieve meaningful goals of reducing prevalence and/or advanced outcomes by 90% in 10 or 15 years.

In all scenarios considered here, the number of patients treated annually with higher SVR therapies would increase from the current SOC, and patients with ≥ F2 fibrosis would access treatment. Scenarios to reduce viremic prevalence would require the treatment of all patients (≥ F0); however, the year in which treatment would become unrestricted (2017 vs. 2020) depends on the desired endpoint (2026 vs. 2031). In addition to reducing prevalence, both scenarios projected a substantial reduction in HCC and liver-related deaths. By comparison, the scenarios designed to reduce advanced outcomes would require a less intensive scale-up of treatment to achieve the desired result, although, the effect on prevalence would be less substantial (35%-55% reduction by 2026, and 55% reduction by 2031).

As previously discussed, there are limitations surrounding the historical inputs used in the model (2-4). A primary concern is a lack of robust and nationally representative epidemiological studies to form a solid historical basis. To address this concern, all inputs used in the model were carefully chosen and agreed upon by the Belgian HCV working group, comprised of local experts in the field of HCV. Moving forward, the working group recommends expanding current data collection systems to improve the availability of quality epidemiological data. For example, e-health is a web-based system of INAMI/RIZIV (Belgian health care authorities) which is used to grant immediate access to treatment, upon request by a physician. In the case of HCV, it currently registers basic patient data (age, sex, genotype, and fibrosis stage) Expanding this system to collect a broader

50%. The cumulative cost savings, compared with the current SOC, would be € 395 M (35%), over 10 years (Fig. 2a).

Scenario 4: Morbidity and mortality prevention (90% reduction in advanced outcomes) in 15 years

In order to reduce advanced stage outcomes by 90% in 15 years, the number of patients treated with higher SVR therapies would need to increase from 900 in 2015 to 3,100 in 2018, with restriction to ≥ F2 patients beginning in 2017. This scenario would result in a 95% reduction in HCV-related HCC and a 90% reduction in liver-related deaths by 2031. In addition, total HCV infections would be reduced by 55% (Fig. 1). The cumulative cost savings, compared with the current SOC, would be € 530 M (30%), over 15 years (Fig. 2b).

Residual risk of HCC

Under the current SOC, there would be 7-15 HCC cases annually among HCV cirrhotic patients achieving SVR during 2016 to 2031 (average = 11). Under the scenarios, there would be 8-36 HCC cases annually among cirrhotic patients achieving SVR (average = 24), regardless of the outcome (prevalence or mortality) or endpoint of interest (2026 or 2031).

Discussion

The HCV therapeutic landscape has advanced rapidly since 2014, with the release of higher SVR therapies and an observed concurrent increase in the number of patients treated in the first quarter of 2015. These advancements have prompted conversations about strategies to reduce the number of HCV infections and HCV-related advanced outcomes. Previous modeling efforts focused on conservative increases in the number of diagnosed and treated patients, and explored the impact of time delays on HCV-related outcomes. The current analysis expands on previous efforts by examining the steps necessary to achieve meaningful goals of reducing prevalence and/or advanced outcomes by 90% in 10 or 15 years.

In all scenarios considered here, the number of patients treated annually with higher SVR therapies would increase from the current SOC, and patients with ≥ F2 fibrosis would access treatment. Scenarios to reduce viremic prevalence would require the treatment of all patients (≥ F0); however, the year in which treatment would become unrestricted (2017 vs. 2020) depends on the desired endpoint (2026 vs. 2031). In addition to reducing prevalence, both scenarios projected a substantial reduction in HCC and liver-related deaths. By comparison, the scenarios designed to reduce advanced outcomes would require a less intensive scale-up of treatment to achieve the desired result, although, the effect on prevalence would be less substantial (35%-55% reduction by 2026, and 55% reduction by 2031).

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Fig. 2. — Estimated cumulative health care cost of current standard of care, with cost savings associated with disease control strategies for a) 10-year strategies, and b) 15-year strategies, excluding the cost of treatment.
range of parameters could not only inform the progress of HCV disease reduction efforts, but could also provide a means to prospectively update and validate the model used for this analysis. In addition, the conduct of an accurate HCV sero-epidemiological study should be considered to validate the current estimations.

It is also possible that we underestimate the overall effect of all scenarios as we don’t take into consideration the reduction on transmission by curing an increasing number of patients.

The Belgian HCV working group recommends working toward the elimination of HCV infections in Belgium over a 15-year time period (Scenario 2). This scenario balances outcomes (90% reduction in viremic prevalence and in HCC and liver-related deaths) with realistic requirements for implementation (gradual increase in treatment and delayed incorporation of patients with no/mild fibrosis).

Several considerations will be necessary before implementing any of the scenarios presented here. Well-organized primary care and an overall implementation of e-health will be prerequisites for early detection and quality of care follow-up. Active screening strategies will also be necessary, as it is estimated that only half of HCV patients are aware of their disease. Moreover, prevention efforts in high risk of transmission-groups (e.g., MSM, IV drug users, prisoners) will be necessary in a scenario of viral elimination. And finally, ethical issues should always be considered when identifying which patients will be excluded from treatment.

In conclusion, this analysis demonstrates that it is possible for Belgium to achieve this reduction by 2031, assuming a commitment is made to significantly increase treatment and diagnosis, utilize higher SVR therapies and expand eligibility to patients without fibrosis. Although the costs of treating a substantially increased number of patients will be high in the short term, it should be taken into account that the long-term impact on cumulative cost burden might be significantly improved.

Author Commentary:

“All of the scenarios presented need to be accompanied by an active screening strategy, since it is estimated that approximately half of the HCV patients are aware of their disease. Moreover, prevention in the groups at high risk of transmission (MSM, drug users, prisoners) will be necessary in a scenario of viral elimination.” — Christophe Moreno

“The costs associated with treating an increasing number of HCV patients are expected to be high. However, from a health economic point of view, the positive societal impact in terms of health gains and potential cost savings related to minimizing the burden of advanced stage disease are considerable. Well-organized primary care and an overall implementation of e-health are, however, prerequisites for early detection and quality of care follow-up.” — Dominique Vandjck

“Although the costs of treating a substantially higher number of patients could be high in the short term, it should be taken into account that the long-term impact on cumulative cost burden might significantly outweigh these former. Insurance companies and government should definitely be made aware of this phenomenon.” — Hans Van Vlierberghe and Wim Lalame

“In addition, ethical issues need to be taken into consideration when identifying which patients will or won’t be treated.” — Pieter Van Damme

“Models depend on the quality of the data that have been used to feed them. There is a lack of recent and good quality epidemiological data in Belgium. Therefore, it is mandatory that health care authorities and health care professionals work together and prospectively collect reliable data to allow validation of the model in the nearer future. The Belgium e-health system may be a suitable tool to achieve this objective.” — Peter Stärkel

References


