Achieving WHO recommendations for Hepatitis C Virus Elimination in Belgium

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Abstract

Background : **The World Health Organization (WHO) released updated guidelines for the screening, care and treatment of patients with chronic hepatitis C virus (HCV) infection.**

Methods : **A previously described HCV disease burden model was used to develop a "WHO scenario" to achieve the WHO recommendations of a 90% reduction in incidence and 65% reduction in liver-related deaths. After determining the steps necessary to achieve this goal, the impact of realistic constraints was modeled.**

Results : **In 2015, there were 66.200 viremic infections, with 43% diagnosed and 1.350 treated. In order to reduce new infections, treatment must be extended to ≥ F0 patients, including people who inject drugs and other individuals at risk of transmitting HCV. Additionally, diagnosis and treatment of 3.030 and 4.060 patients, respectively, would be required. The largest attenuation of the WHO scenario would occur if no new cases were diagnosed after 2018 (300% more viremic infections by 2030). Limiting treatment to ≥ F2 patients or treating fewer patients (3.000) would result in 220% or 140% more viremic cases, respectively, compared with the WHO scenario.**

Conclusions : **Achieving the WHO guidelines in Belgium requires a coordinated effort to scale up treatment and prevention efforts and to allow treatment access to patients of all fibrosis**

stages. A scale-up of treatment, however, requires patients to be both diagnosed and linked to care, suggesting a need for increased awareness and expanded screening efforts. Finally, prevention of new HCV infections requires a comprehensive understanding of the population at risk of transmitting HCV. (Acta gastroenterol. belg., **2016**, 79, **222-226**).

Key words : hepatitis C virus, treatment, screening, elimination.

Background

The Belgian Working Group for HCV has spent the last few years compiling and analyzing epidemiological data (as available) surrounding hepatitis C virus (HCV) infection in Belgium. These efforts have used a well-established HCV disease burden model, following a standard methodology (1-4), to forecast the anticipated disease burden associated with untreated HCV and to see the impact of modeled scenarios to increase treatment and diagnosis rates (5-8). Historically, modeled scenarios were developed through group consensus to achieve goals of elimination and/or prevention of mortality. The present analysis seeks to achieve targeted goals proposed by the World Health Organization (WHO) in a draft guidance for a health sector strategy for the elimination of HCV.

Though still under discussion until May 2016, The proposed guidance recommends that countries work toward a 90% reduction in incidence of HCV as well as a 65% reduction in liver-related deaths by 2030, while increasing diagnosis rates and treatment eligibility. With the introduction of all oral, interferon-free regimens, the treatment rate in Belgium nearly doubled from 2014 to 2015. Treatment access was limited to patients with advanced fibrosis (≥ F3), which is projected to remain the case into 2016 and to be expanded to ≥ F2 in 2017.

In order to meet WHO recommendations for the prevention of new infections, treatment of early stage patients (F0-F2) as well as high-risk populations must be considered. In April 2016, WHO released recommendations for the screening, care and treatment of HCV infected individuals and identified four groups in whom treatment should be prioritized (9) : 1) patients at increased risk of death (≥ F3, post-liver transplant, etc.), 2) patients at risk of accelerated fibrosis (coinfection with HIV or HBV, metabolic syndrome, etc.), 3) patients with severe extrahepatic manifestations, 4) patients in whom treatment could maximize the reduction in incidence (people who inject drugs [PWID] and those with increased risk of transmission, HCV infected mothers, incarcerated populations, hemodialysis patients and health care workers) (9).

The populations at greatest risk for new infections – the incarcerated population, PWID and HIV positive men who have sex with men (MSM) – are also at greatest risk of not receiving treatment due to stigmatization (10). Recent modeling efforts suggest that PWID account for nearly half of incident infections in Belgium, while MSM

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account for nearly a quarter. Reaching this population with treatment and harm reduction efforts is imperative for achieving WHO recommendations for the reduction in new infections.

Given the recent guidelines and the expanding treatment landscape, an updated analysis was conducted to identify the steps necessary to achieve WHO recommendations for a 65% reduction in liver-related deaths alongside a 90% reduction in new infections. While not achieving this goal, the impact of treating 3.000 patients annually was considered. And finally, the impact of not treating early stage patients, including those at risk for transmission and re-infection, was considered.

Methods

A previously described Microsoft Excel-based model was populated with Belgian data, and scenarios were developed to explore the steps necessary to achieve WHO recommendations for reduction in liver-related deaths and new infections by 2030 (2-4,10).

Historical Base : Prior to 2015, treatment with 24 or 48 weeks of Pegylated Interferon (Peg/IFN) and Ribavirin (RBV) was the standard of care, with sustained viral response (SVR) rates of 40%-65% (12,13). Treatment was focused on METAVIR fibrosis stage ≥ F2 patients with genotype (G)1, G3 and G4, and ≥ F0 patients with G2. Approximately 710 patients were treated annually during this time (11).

Current standard of care (SOC) : Beginning in 2015, direct-acting antiviral therapy (DAAs) with SVR rates of 95% became available in Belgium. In this year, the number of treated patients increased to 1.350, and treatment was focused primarily on patients with advanced fibrosis (≥ F3). The 2015 treatment paradigm has been slated to continue into 2016, however first-quarter results from the eHealth database suggest that only 1.080 ≥ F3 patients will be available to treat. Expansion of treatment to include all patients ≥ F2 is estimated to occur in 2017 (11).

WHO scenario : From 2017 forward, a scenario was developed to achieve the proposed WHO recommendations for diagnosis and prevention of HCV, alongside a > 65% reduction in liver- related deaths. Within the model, the number of treated and diagnosed patients was increased until the proposed conditions were met. To avoid overlooking the impact of 2015 treatment efforts, the WHO scenario was developed against the 2030 projections from the historical base.

Scenario sensitivity analysis : After the optimal scenario was developed to achieve proposed WHO recommendations, a sensitivity analysis was run on key variables to identify their impact. Treating a maximum of 3.000 patients, discontinuing diagnosis and limiting treatment to ≥ F2 patients were all considered.

Results

Summary of the infected population in 2015

In 2015, there were an estimated 66,200 (95% UI 24.200-77.600) viremic infections in Belgium, approximately 43% (95% UI 23%-55%) of which were diagnosed (Fig. 1). In 2015, an estimated 1.350 patients were treated, with 2,280 viremic cases newly diagnosed (Fig. 1).

WHO Scenario

In order to achieve a 65% reduction in liver-related deaths and a 90% reduction in new infections by 2030 (Fig. 2), the number of patients treated with higher SVR therapies would need to be increased annually, from 1.350 in 2015 to 4.060 beginning in 2018. Diagnosis

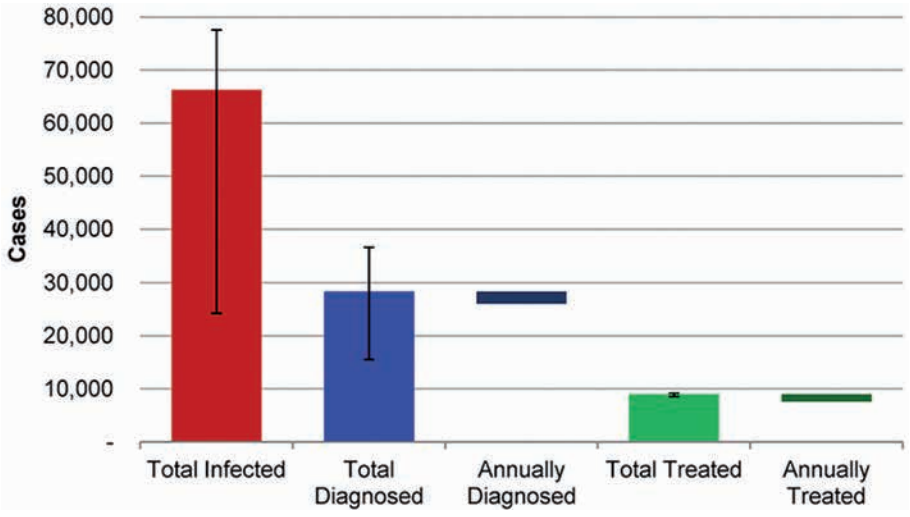

Fig. 1. — Cascade of care, including total viremic cases, total diagnosed (historical), annually diagnosed, total treated (historical) and annually treated, for 2015.

Table 1. — **Impact on viremic cases and liver related deaths in 2030, by scenario, compared with the WHO scenario – WHO) 90% reduction in new cases and 65% reduction in liver-related deaths by 2030; Scenario 1) Limiting treatment to 3.000 patients; Scenario 2) Discontinuing diagnosis after 2018; Scenario 3) Limiting treatment to ≥ F2 patients after 2018**

	2015 Estimate	2030 Estimate	% change compared with WHO Scenario
Viremic Cases			
WHO Scenario	66.200	6.800	–
Scenario 1	66.200	16.300	140%
Scenario 2	66.200	27.300	300%
Scenario 3	66.200	21.800	220%
Liver-related deaths			
WHO Scenario	365	175	–
Scenario 1	365	245	40%
Scenario 2	365	260	50%
Scenario 3	365	130	**-25%**

rates would need to increase 10% each year beginning in 2016, to achieve a total of 3.030 patients diagnosed annually by 2018. Additionally, treatment would be available to ≥ F2 patients in 2017 and all patients (≥ F0) beginning in 2018. Under this scenario, there would be 6.800 viremic cases in 2030, with 175 liver-related deaths (Table 1).

Scenario sensitivity analysis : Treat 3.000 patients annually

Limiting the number of treated patients to 3.000 annually beginning in 2018 would result in 40% more liver-related deaths and 60% more prevalent HCC cases, as compared to the WHO scenario (Table 1). Furthermore, total viremic cases would be 1.4-fold higher by 2030 than under the WHO scenario (Fig. 2).

Scenario sensitivity analysis : No diagnosis after 2018

After 2018, if no new cases are diagnosed, treatment of 4.060 patients annually will be sustainable until 2024. By 2030, only 20 patients would be diagnosed and available to treat, with 27.300 undiagnosed viremic cases remaining. Additionally, this would result in 50% more liver-related deaths and 85% more HCC cases, as compared to the WHO scenario (Table 1).

Scenario sensitivity analysis : Treat ≥ F2 only

Limiting treatment to ≥ F2 patients, while continuing to treat 4.060 patients and diagnose 2.280 patients annually would result in 25% fewer liver-related deaths and HCC cases, as compared to the WHO scenario (Table 1). Total viremic cases, however, would be 2.2-fold higher by 2030 (Fig. 2).

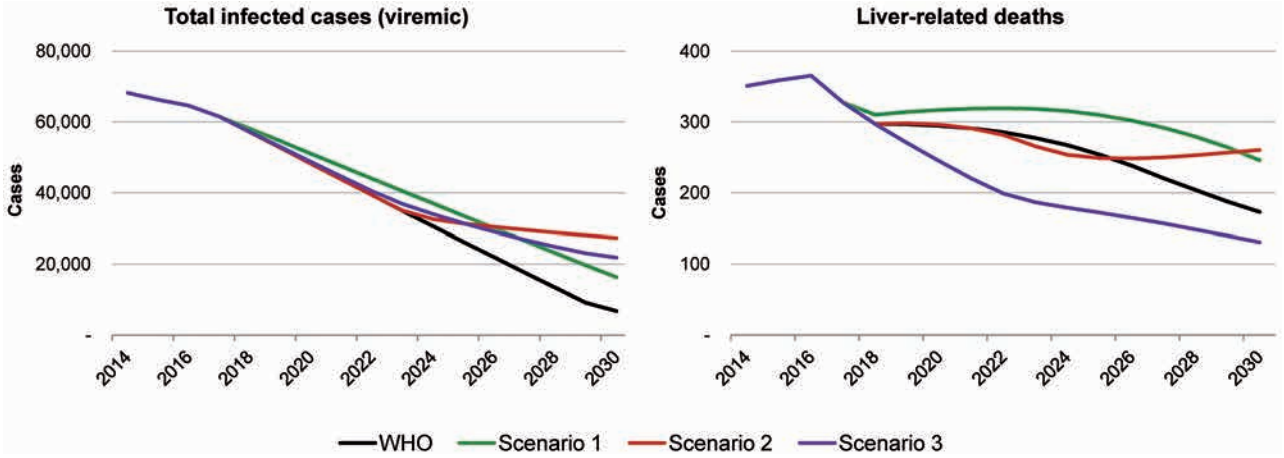

Fig. 2. — Viremic cases and liver-related deaths, by scenario – **WHO)** 90% reduction in new cases and 65% reduction in liver-related deaths by 2030 ; **Scenario 1**) Limiting treatment to 3.000 patients ; **Scenario 2**) Discontinuing diagnosis after 2018 ; **Scenario 3**) Limiting treatment to ≥ F2 patients after 2018.

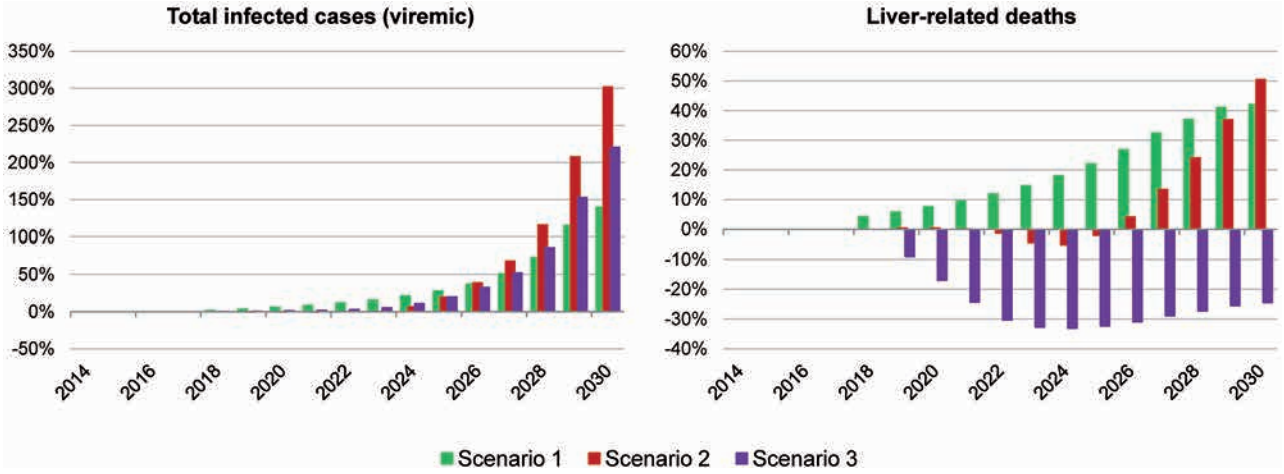

Fig. 3. — Scenario sensitivity – impact of reduced treatment, discontinued diagnosis and fibrosis restrictions, as compared with the WHO scenario – **Scenario 1**) Limiting treatment to 3.000 patients ; **Scenario 2**) Discontinuing diagnosis after 2018 ; **Scenario 3**) Limiting treatment to ≥ F2 patients after 2018.

Discussion

Achieving WHO recommendations for the reduction of liver-related deaths and new infections is possible in Belgium through the treatment of up to 4.060 persons annually by 2018. Treatment of ≥ F0 patients is necessary beginning in 2018, and diagnosis of 3.030 cases annually (2.280 diagnosed in 2015) is necessary by 2018. Finally, in order to achieve a 90% reduction in new infections, annual treatment of people who are currently injecting is required alongside efforts to prevent new infections in the general and HIV+ MSM populations.

Implementation of the scenarios presented here should be complemented with awareness campaigns, a concerted effort to stage previously diagnosed patients and systems to encourage linkage to care. In order to focus treatment on advanced-stage patients, accurate staging and referral of these patients is first necessary. Development of a national registry system may provide an opportunity to prospectively track the success of treatment and screening strategies.

Reducing new infections by 90% requires a thorough understanding of the sources of new infections. In this analysis, new infections were assumed to occur primarily among actively injecting PWID who share injecting equipment, accounting for approximately half of new infections but fewer than 5% of total cases. MSM with risky sexual practices account for nearly a quarter of new infections and fewer than 5% of total cases. The remainder of new infections may occur through vertical or nosocomial transmission, or be of unknown origin. For the purposes of this analysis, WHO goals for reducing new infections were assumed to refer to the transmission of HCV occurring within the country. Thus, the impact of new cases due to immigration was incorporated into the model, but was excluded in calculating incidence reduction goals.

Reducing new infections among actively injecting PWID requires the expansion of harm reduction services to promote the use of sterile syringes and to encourage a reduction in injecting frequency. HCV treatment without a concurrent effort to change injecting behaviors is likely to result in increased re-infection from exposure to HCV in injecting networks (12). Similarly, continued high-risk sexual practices may result in HCV re-infection among MSM (13). Awareness campaigns and concerted prevention efforts should be employed to prevent new infections and re-infections in these populations. Additionally, timely, high-coverage treatment of the population at-risk can reduce the viral pool and minimize the chance of re-infection (14).

In conclusion, this analysis demonstrates that a comprehensive, long-term strategy for Belgium can achieve both a 65% reduction in liver-related deaths and a 90% reduction in HCV incidence. The success of this strategy, however, is contingent on improved case finding and linkage to care and the treatment of patients at greatest risk of transmitting HCV. Increased awareness among the general population is recommended to improve diagnosis rates, and increased awareness among general practitioners is recommended to improve referrals and linkage to care.

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