CHRONIC HEPATITIS C IN THE CZECH REPUBLIC: FORECASTING THE DISEASE BURDEN

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SUMMARY

Objective: Chronic HCV infection is associated with cirrhosis of the liver, hepatocellular carcinoma (HCC), and liver transplantation. HCV disease burden and the impact of new potent direct acting antivirals (DAAs) in the Czech Republic are unknown.

Methods: Using a modelling framework, HCV disease progression in the Czech Republic was predicted to 2030 under the current standard of care treatment structure. In addition, two strategies to reduce the future burden of HCV infection were modelled: an incremental increase in treatment annually and WHO targets.

Results: The number of viremic infected individuals in the Czech Republic is estimated to peak in 2026 (n = 55,130) and to decline by 0.5% by 2030 (n = 54,840). The number of individuals with compensated cirrhosis (n = 1,400), decompensated cirrhosis (n = 80), HCC (n = 70), and liver-related deaths (n = 60) is estimated to more than double by 2030. Through aggressive increases in diagnosis and treatment, HCV related mortality may decrease by 70% by 2030.

Conclusions: Disease burden associated with chronic HCV infection is projected to peak in the Czech Republic in 30–40 years. Assuming that the current portion of DAAs used remains constant, a significant reduction in HCV disease burden is possible through increased diagnosis and treatment through 2030. This analysis provides evidence in order to facilitate the development of national strategies for HCV care and management in the Czech Republic.

Key words: hepatitis C, disease burden, epidemiology, Czech Republic

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https://doi.org/10.21101/cejph.a5350

INTRODUCTION

Infection associated with chronic HCV is a major cause of liver disease in Europe (1). In the Czech Republic, compared with other European countries, the HCV epidemic began later owing to geographical barriers, limited immigration from neighbouring endemic countries and a delayed surge in injection drug use. However, in recent years, HCV infection has become one of the leading causes of liver transplantation in the Czech Republic (2). As the infected cohort ages, the burden of HCV-related disease is expected to increase greatly.

The Czech Republic is a low-endemic country for HCV infection with reported anti-HCV positivity estimates between 0.2–1.0% (3–5); nevertheless, little is known on the national level regarding current and future disease burden. There is no general screening programme in the Czech Republic. To date, only specific subgroups are screened on a regular basis. These groups include: blood donors, healthcare workers, patients on maintenance hemodialysis, prisoners and drug users starting weaning programmes. HCV prevalence varies widely between these groups with the lowest prevalence reported among blood donors in Prague (0.13%) and the highest prevalence reported among injection drug users (IDU) (58.6%) (6, 7).

In the Czech Republic, interferon-free direct-acting antiviral (DAA) combinations were approved for reimbursement in 2014. The current standard of care in the Czech Republic allows for unrestricted treatment; however, in light of the aforementioned factors and cost of DAAs and budget restrictions, those that are older and that have progressed further are prioritized. With the introduction of new generations of DAAs, treatment has resulted in higher sustained virological response (SVR) rates, fewer side effects and more simple regimens.

In this study, a modelling approach was used to analyze the progression of HCV disease burden in the Czech Republic; to assess two strategies for addressing chronic HCV infection: the effects of incremental increases in treatment and aggressive diagnosis and treatment; and to review the impact of these strategies on future disease burden, considering strategy implementation.

MATERIALS AND METHODS

A detailed description of the model and methodology has been reported on extensively (8). The infected HCV population was characterized using published literature, Czech Government reports and estimates from a panel of the country experts. Czech population data were obtained by 5-year age and gender cohorts from the United Nations World Population Prospects (9). Estimates of historic and future population were obtained for the years 1950–2100.

Baseline Population Characteristics

Current anti-HCV prevalence for the general population was estimated using a recent prospective multicentre observation seroprevalence study of 3,000 healthy adult subjects aged 18 and older (5). The HCV prevalence was estimated by taking into account the number of people who inject drugs, and the age and gender distribution of all included populations in the study. The viremic prevalence in the general population in the Czech Republic was estimated to be 0.5% (0.2–0.63%) in 2015 (5). As all reported HCV cases were RNA positive, the viremic rate was set to 100%. The age and gender distribution was developed using data from 2015, supplied by The National Institute of Public Health, which were reported to the EPIDAT system (Fig. 1) (10). Genotype studies in the Czech Republic are often limited to selected populations such as blood donors (11) and IDUs (3, 12). The genotype distribution (Table 1) was reported by Nemecek et al. (4, 11) and Chlibek et al. (5) estimating a relatively even split between genotype 1 and genotype 3.

In 1998, blood transfusion was reported as a risk factor of HCV transmission in 15.0% of patients (13). Transmission of HCV infection through transfusion has been declining since 1992 after introduction of blood donors screening and is no longer considered a risk factor for transmission. The most common route of HCV transmission in the Czech Republic is through injection drug use. In 2015, 51.1% of injection drug users were found to be positive for anti-HCV (5). In 2015, it was estimated that 15.6% of prevalent cases were current injection drug users (5, 7).

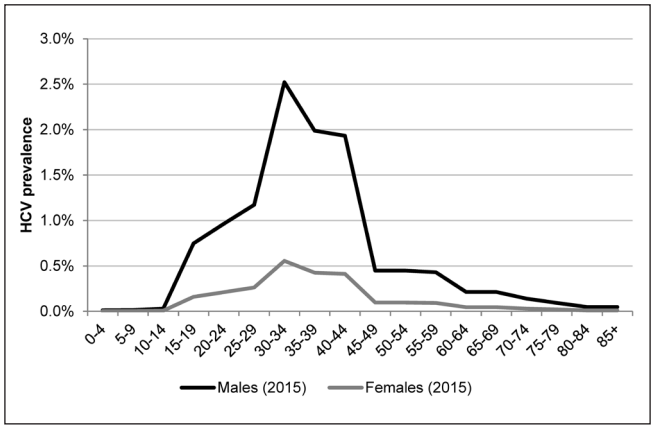

***Fig. 1**. Age and gender distribution of anti-HCV prevalence in the Czech Republic, 2015.*

There is limited data available on the incidence of new cases of HCV in the Czech Republic. An incidence curve for the estimation of new cases was developed based on discussions regarding the natural history of HCV disease in the Czech Republic with the expert panel. The annual number of new cases in the Czech Republic is considered to have peaked in 2009 before decreasing. It is believed that the number of new cases arising annually is relatively stable in light of continued transmission through intravenous drug usage. In 2016, there were estimated 1,740 new cases of reported acute and chronic HCV in the Czech Republic. The data described above are summarized in Table 2.

Mortality and Liver Related Morbidity

Background mortality for the years was collected by five-year age and gender cohorts using the United Nations Population Database (9). Increased mortality among the transfusion-acquired HCV and IDU-acquired HCV was accounted for by applying a standard mortality rate of 2.1 and 10.0, respectively, for the affected age groups (14–20). Age and gender specific transition probabilities were used to progress patients annually through each disease state. A more detailed description has been described elsewhere (8).

Liver transplant data from 2001–2013 was available through the International Registry on Organ Donation and Transplantation (IRODaT) (21). Transplant data from 2013–2016 was available from the transplant centres (22). In 2016, there were 177 liver transplants performed in the Czech Republic with 18 being due to HCV. In all years prior to 2013, it is estimated that 15.6% of transplants are attributable to HCV (2).

Modeled Base Case and Treatment Strategies

A base case and two treatment strategies, incremental increase in treatment and WHO targets, were modelled in the Czech Republic.

It is estimated that in 2016, 910 patients were treated in the Czech Republic, with the majority being treated with DAAs. DAAs were first introduced in the Czech Republic in 2014, thus allowing for an increased patient eligibility pool. Audit data was used to estimate the total number of treated patients in 2015 and 2016. The total number of treated patients decreased from approximately 1,050 in 2015 to 910 in 2016, but the number treated with DAAs increased from 270 to over 570.

In 2015, there were estimated to be 17,300 viremic individuals in the Czech Republic living with a diagnosis. Each year, an estimated 1,100 viremic individuals are newly diagnosed (5, 10). Treatment and diagnosis estimates for 2015 are shown in Table 2.

In the base case, the estimates of SVR rates were based on real-life SVR, clinical studies and expert opinion (23–27). There are currently no treatment restrictions based on age; however, treatment is restricted to those ≥F1. The efforts for the strategies outlined below assume that no further restrictions will be enacted.

***Table 1**. HCV genotype distribution in the Czech Republic, 2015*

Genotype	1a	1b	1 other	2	3	4	5	6
Percent	26%	26%	0%	0%	48%	0%	0%	0%

Table 2. *Model inputs and 2016 estimations*

	Historical (min max uncertainty interval)	Year	2016 (Est.)
HCV infected cases	53,200 (21,300–67,000)	2015	53,500
Total viremic cases	53,200 (21,300–67,000)	2015	53,500
Viremic prevalence	0.5% (0.2–0.6%)		0.5%
HCV diagnosed (viremic)	17,300	2015	17,400
Viremic diagnosis rate	32.5%		32.5%
Annual newly diagnosed	1,100	2016	1,100
New infections			1,740
New infection rate (per 100,000)			16.0
Treated			
Number treated	900	2016	910
Annual treatment rate	1.7%		1.7%
Risk factors			
Number of active IDU with HCV			8,300
Percent active IDU			15.6%
Previous blood transfusion			0
Percent previous blood			0.0%
Liver transplants			
Total number of liver transplants	177	2016	
Liver transplants due to HCV	18	2016	
Annual number cured	800	2016	
Average SVR rate	90%	2016	
General population*	10,565,284	2015	

HCV – hepatitis C virus; IDU – intravenous drug user; SVR – sustained virological response; *Mid-year population in 2016 according to the Czech Statistical Office.

In the Czech Republic, there is a planned increase in treatment of 10% annually owing to the regular annual increase in budgets allocated for HCV therapy by healthcare payers. In order to observe the effects of a slightly more aggressive strategy a scenario has been created that increases the number treated by 15% annually while keeping the SVR the same as the base case. By 2025, the number of individuals diagnosed annually must be increased to 2,130 in order to keep pace with the number of treated patients.

To significantly reduce HCV burden in the Czech Republic, a second strategy with aggressive diagnosis and treatment strategy was developed to achieve the WHO targets of 90% of the infected population being diagnosed and 65% reduction in liver related mortality (28). Beginning in 2019, screening efforts (29) result in 2,000 new diagnoses per year, a 100% increase from 2015, with an associated 200% increase in treatment across genotypes to 3,000 patients. To achieve reductions, additional increases in diagnosis and treatment were applied in each subsequent wave. By 2024, an estimated 3,500 patients will receive treatment annually and expand to 4,900 patients treated in 2025. This figure continues through 2030.

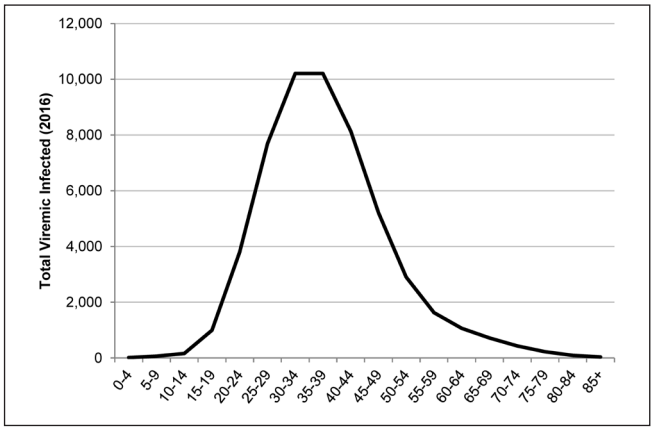

Fig. 2*. Total viremic cases by age, 2016 (base case model output).*

RESULTS

Base Case

In 2015, there were estimated 53,200 infected individuals in the Czech Republic. The age distribution of the 2015 viremic population with chronic HCV is shown in Figure 2. By 2030, as the infected cohort ages, liver-related mortality is forecasted to increase by 100%.

The viremic infected population is anticipated to peak in 2026 with 55,130 individuals (Figures 3 and 5). By 2030, the number of individuals progressing to decompensated cirrhosis, hepatocellular carcinoma (HCC), and liver-related deaths will increase by 146% and 77%, and 116%, respectively, from 2015 (Figures 4 and 5).

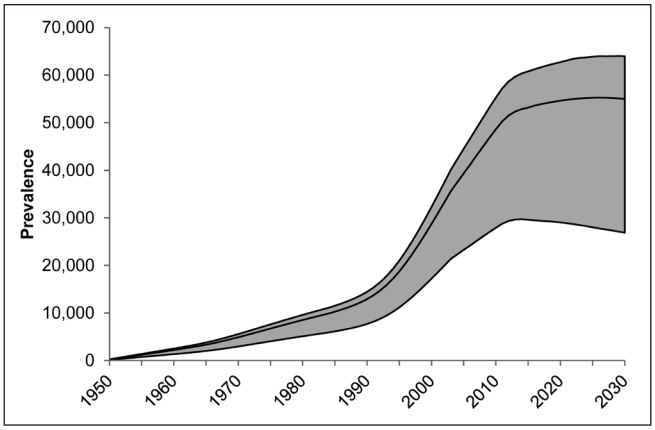

***Fig. 3**. Total viremic cases by year, 1950–2030 (base case model output).*

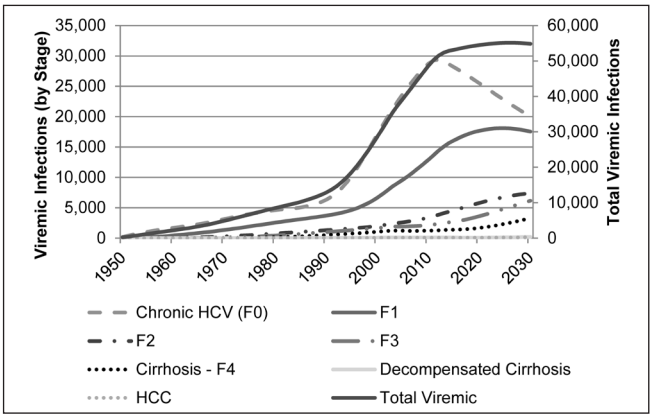

***Fig. 4**. Number of viremic cases in total and by disease stage, 1950–2030 (base case model output).*

Incremental Increase in Treatment

The total viremic population is forecasted to decrease at a faster rate than under the base case scenario, with 39,900 viremic individuals in 2030 corresponding to a 25% decrease (Figures 3 and 5). In this scenario, HCV related mortality would decrease by 41% by 2030 corresponding to 480 lives saved.

Additionally, by 2030, the number of individuals with decompensated cirrhosis will decrease to 40 individuals, and the number of HCC cases will decrease to 100, a 52–59% improvement over the base case forecast for 2030 (Fig. 5).

WHO Targets

Based on WHO elimination strategy (28), modelling an aggressive diagnosis and treatment strategy resulted in an 81% reduction in the total viremic population by 2030 with only 10,000 cases remaining in 2030. This strategy results in a 70% decrease in HCV-related mortality, correlating to 640 lives saved.

By 2030, the number of individuals with decompensated cirrhosis will decrease to fewer than 20 individuals and the number of individuals with HCC to fewer than 20.

DISCUSSION

Modelling has been demonstrated to be effective in predicting HCV disease burden. In the present study, a modelling approach to forecast the future burden of HCV related liver disease through 2030 was used for the Czech Republic. Using data derived from published literature, unpublished government reports and expert opinion, it forecasted that the infected viremic population in the

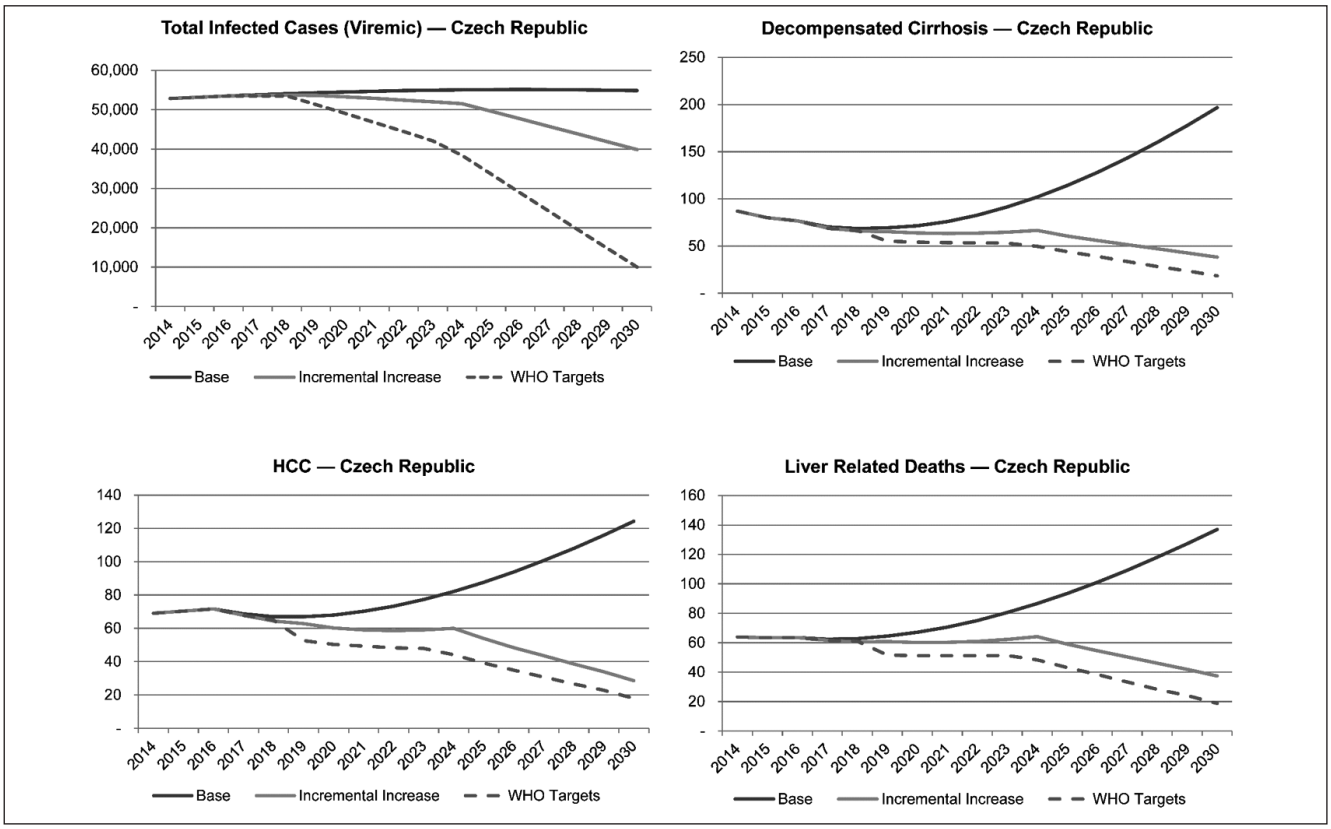

***Fig. 5**. Morbidity and mortality by strategy and by year, 2013–2030.*

Czech Republic is increasing with a peak prevalence of 55,130 infected individuals in 2026 before beginning to decline.

While keeping the same treatment efficacy, but increasing treatment annually by 15%, a moderate reduction, 25%, in the total number of viremic infections will occur. Nevertheless, by keeping the fibrosis restriction at ≥F1, the HCV related morbidity and mortality are expected to decrease by up to 59%. In order for this scenario to take place, there would need to be an increase in screening starting in 2025.

A strategy was modelled wherein aggressive increases in screening and treatment were applied to achieve WHO targets (28). Assuming an increase in screening and treatment, the total viremic infected is anticipated to decrease to 10,000 infected individuals in 2030. This reduction assumes no fibrosis staging or age restrictions starting in 2019. Moreover, it assumes an increase in diagnosis from 960 individuals a year in 2015 to just over 6,200 individuals by 2025.

A reliable general screening programme is crucial to HCV elimination in the Czech Republic. Both increases in diagnosis and treatment must be implemented to achieve significant reductions in disease burden. Czech screening programmes that have already been adopted have contributed significantly to a decrease in nosocomial transmission of HCV infection. For example, in patients on maintenance hemodialysis, there has been a decrease in anti-HCV prevalence from 30% in the 1990s to less than 5% to date (30). With rapidly evolving care for HCV patients and increasingly effective and tolerated all-oral antiviral regimens, all patients identified by means of screening programmes could receive antiviral treatment. Based on the recommendations for birth cohort screening developed by the Centers for Disease Control and Prevention (CDC) in the United States, the most effective screening programme in the Czech Republic would be to target individuals born between 1958 and 1993 (31). This population cohort reflects 70% of the infected viremic population.

A limitation of this analysis is the unknown future genotype structure in the Czech Republic. Historically, genotype 1b was the most prevalent genotype in the Czech Republic. More than 90% of treated individuals in the 1990s and 99% of patients indicated for liver transplantation for HCV infection from 1995 to 2013 were infected with genotype 1 (2, 32, 33). In addition, more than 50% of viremic patients in the Czech Republic have low pretreatment viremia, representing a positive predictive factor of response to treatment. Most Czech centres reported an SVR rate 55−60% with Peg-IFN-α and ribavirin treatment in the cohorts of genotype 1b patients, slightly higher than SVR rates reported in clinical trials (30). However, owing to immigration from endemic countries and increasing HCV prevalence among IDUs over the last 20 years, the rate of genotype 3 in new HCV cases is rising: 31.1% in 2012 and 46.4% in 2015, whereas the proportion of other genotypes (G2, G4, etc.) is negligible (5, 11). Fortunately, the new generation direct-acting antivirals are pangenotypic with an excellent efficacy across genotypes and independently of pretreatment viremia (34), therefore, we do not presume a lower treatment efficacy in genotype 3 patients.

CONCLUSIONS

Owing to a later onset of peak infectivity, the Czech Republic is in a unique situation to curb the coming epidemic of HCV morbidity and mortality providing there is a commitment to large scale screening with linkage to care.

Conflict of Interests

None declared

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Received March 25, 2018
Accepted in revised form April 25, 2019