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SUPPLEMENT ARTICLE

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Strategies to manage hepatitis C virus infection disease burden—Volume 4

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Abbreviations: DAA, direct-acting antiviral agent; G, Genotype; GHSS, Global Health Sector Strategy on viral hepatitis; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; IDU, injection drug use; Peg-IFN, Pegylated interferon; RBV, ribavirin; SVR, sustained viral response; WHO, World Health Organization.

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Summary

The hepatitis C virus (HCV) epidemic was forecasted through 2030 for 17 countries in Africa, Asia, Europe, Latin America and the Middle East, and interventions for achieving the Global Health Sector Strategy on viral hepatitis targets—"WHO Targets" (65%

reduction in HCV-related deaths, 90% reduction in new infections and 90% of infections diagnosed by 2030) were considered. Scaling up treatment and diagnosis rates over time would be required to achieve these targets in all but one country, even with the introduction of high SVR therapies. The scenarios developed to achieve the WHO Targets in all countries studied assumed the implementation of national policies to prevent new infections and to diagnose current infections through screening.

KEYWORDS

diagnosis, disease burden, elimination, epidemiology, hepatitis C virus, hepatitis C, incidence, mortality, prevalence, scenarios, strategy, treatment

1 | INTRODUCTION

Although the number of new hepatitis C virus (HCV) infections has declined in recent years, liver-related morbidity and mortality are on the rise due to an ageing infected population.[1] The availability of more efficacious treatment options has the potential to influence the treatment paradigm at a country level. In the light of these new treatments and the possibility of elimination, the World Health Organization's 69th World Health Assembly approved the Global Health Sector Strategy (GHSS) on viral hepatitis.[2] The strategy includes a set of targets for countries to achieve including a diagnosis rate of 90% of total infections, a 90% decrease in new infections and a 65% decrease in liver-related mortality by 2030.

In this study, a modelling approach was used to forecast the future disease burden and to develop a "WHO target" scenario for each country to meet the GHSS targets. The findings are not meant to prescribe specific strategies for implementation but rather to serve as "what-if" scenarios to support long-term strategic planning efforts to reduce the disease burden associated with HCV.

2 | METHODOLOGY

Previous publications have provided technical details of the model used to forecast HCV disease burden.[3,4] An interactive model interface allowed for the adjustment of several parameters: the number of patients treated, the proportion of cases eligible for treatment, the extent of treatment restrictions, the average sustained viral response (SVR) by genotype, the number of newly diagnosed individuals and the number of new infections at five different points in time.

A variety of therapies were available in 2015, including direct-acting antivirals (DAAs) with or without pegylated interferon (Peg-IFN) and/or ribavirin (RBV), dual therapy (Peg-IFN/RBV) and triple therapy regimens using protease inhibitors. Over the last few years, many countries have experienced a period of transition in which a combination of low and high SVR therapies was used. This was represented in the model by changing the average SVR parameter. The average SVR for each genotype in 2015 was determined using a weighted average based on the proportion of treated patients that were treated with DAAs compared to those treated with Peg-IFN/RBV, when these data were available. If a country exclusively treated patients using oral DAAs, this was reflected in a higher average SVR for each genotype.[5]

The future number of treated patients was limited by the number of diagnosed, eligible and unrestricted cases. Restrictions were defined implicitly (by physician's practice) and/or explicitly (by treatment guidelines) and could be modified in the model by changing the upper and lower end of patient's age and the stage of fibrosis (≥F4, ≥F3, ≥F2, ≥F1 or ≥F0). While age restrictions were applied to all genotypes, the restrictions by the stage of liver disease were applied to specific genotypes. Patients with decompensated cirrhosis, irrespective of genotype, were considered ineligible for any treatment that involved Peg-IFN. The fibrotic stages eligible for treatment are shown in Figures 1-17. When the number of treated patients was greater than those diagnosed, eligible and unrestricted, the number of newly diagnosed cases was increased or the treatment restrictions were relaxed. The focus of the analysis was to highlight how many cases have to be diagnosed to achieve a strategy rather than to forecast the screening capacity in a country. When treatment data for 2015 were not available, it was assumed that the number of treated patients in 2015 was equal to the number of treated patients in 2014.

In this analysis, two strategies were considered; base and WHO target. In the base strategy, all assumptions (the number of acute cases, treated patients, per cent of patients eligible for treatment, treatment restrictions, the number of newly diagnosed patients and the average SVR by genotype) were projected to remain constant after 2015. While it is unlikely that the treatment paradigm will remain completely unchanged over the years, this scenario serves as a reference to compare against. The base scenario for each country was described in detail previously.[4] The WHO target scenario achieves WHO GHSS targets of a 90% reduction in new infections and a 65% reduction in liver-related mortality by 2030. To meet these targets, screening and treatment were expanded across all genotypes and treatment restrictions were changed in future years.

Figures 1-17 detail the scenario inputs, including SVR, fibrosis stage and medical eligibility by age and genotype, as well as the number of patients that must be diagnosed and treated to meet the WHO targets.

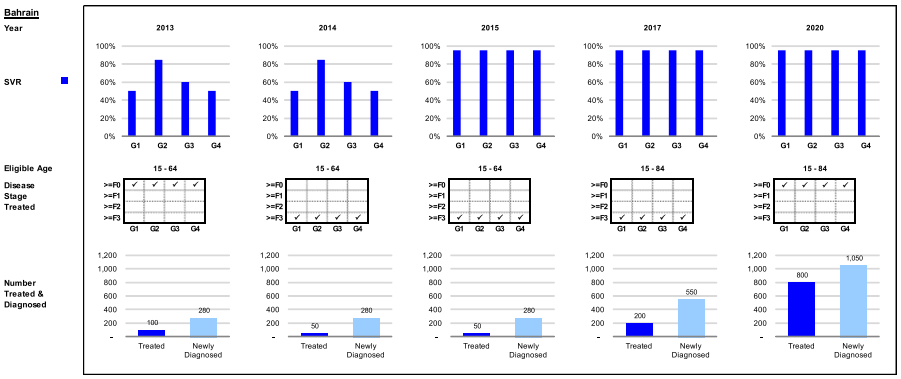

FIGURE 1 Bahrain model inputs, by year

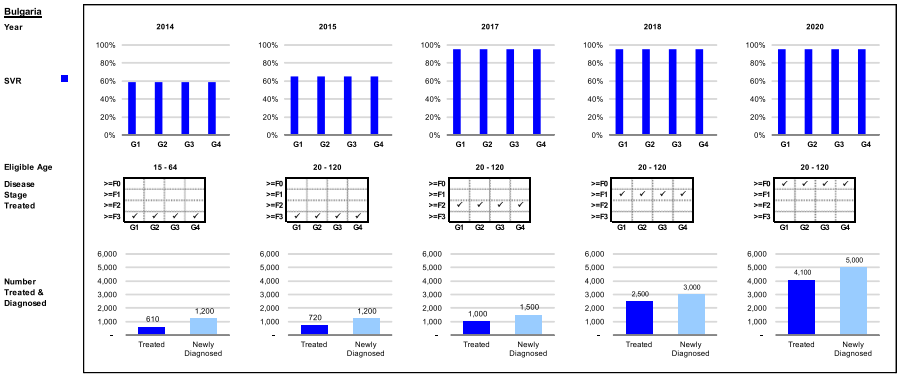

FIGURE 2 Bulgaria model inputs, by year

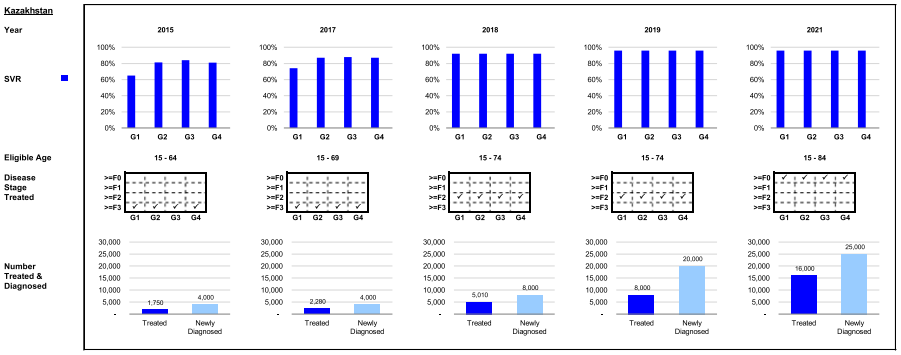

FIGURE 3 Cameroon model inputs, by year

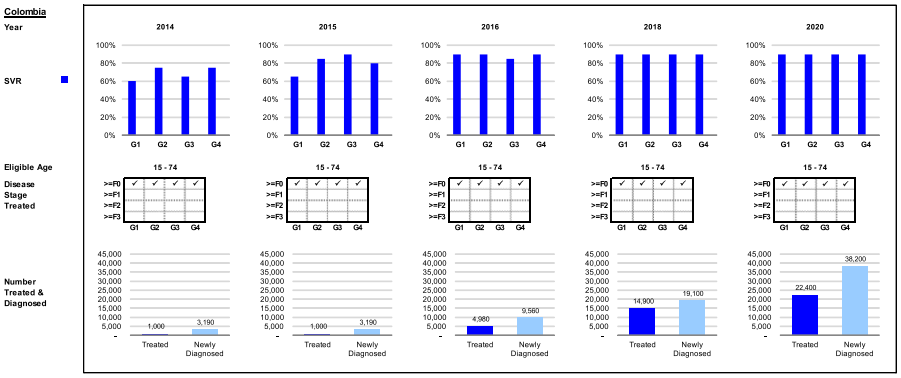

FIGURE 4 Colombia model inputs, by year

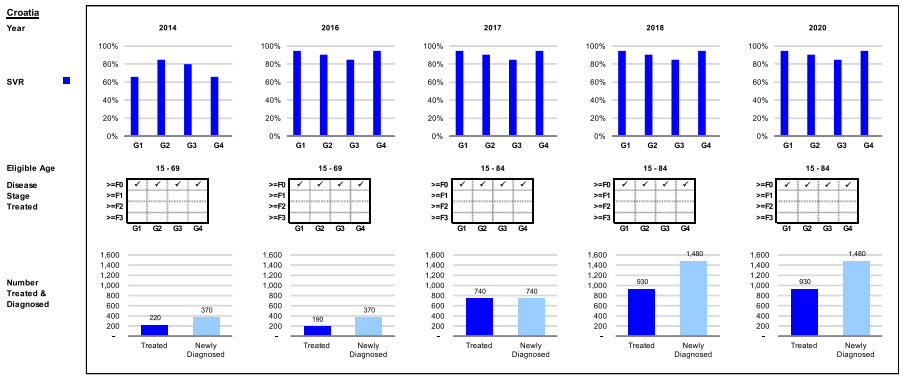

FIGURE 5 Croatia model inputs, by year

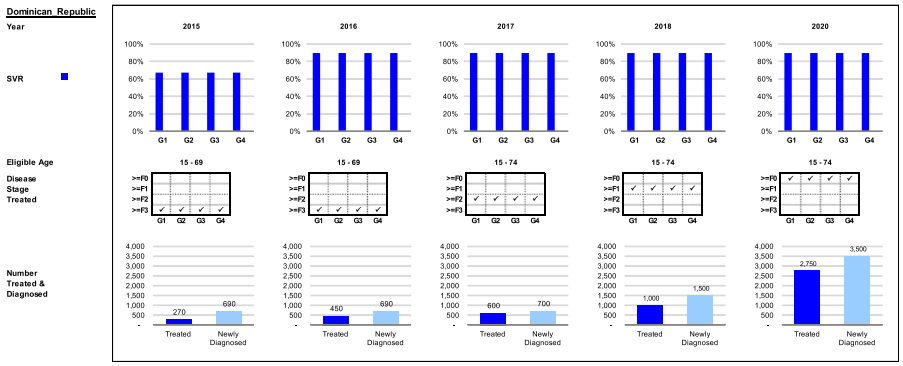

FIGURE 6 Dominican Republic model inputs, by year

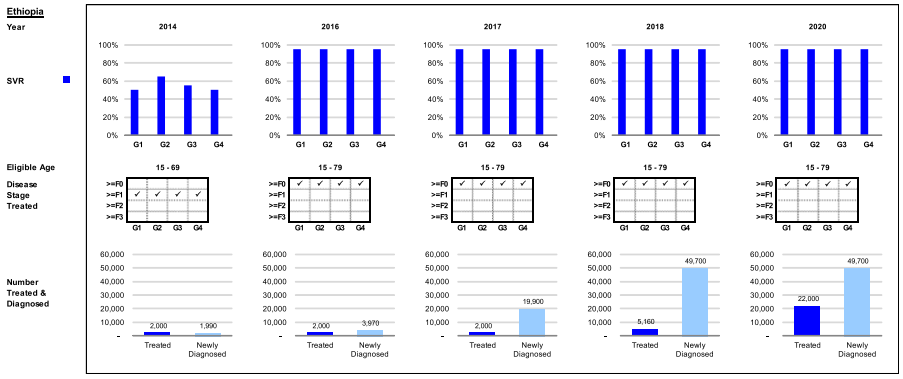

FIGURE 7 Ethiopia model inputs, by year

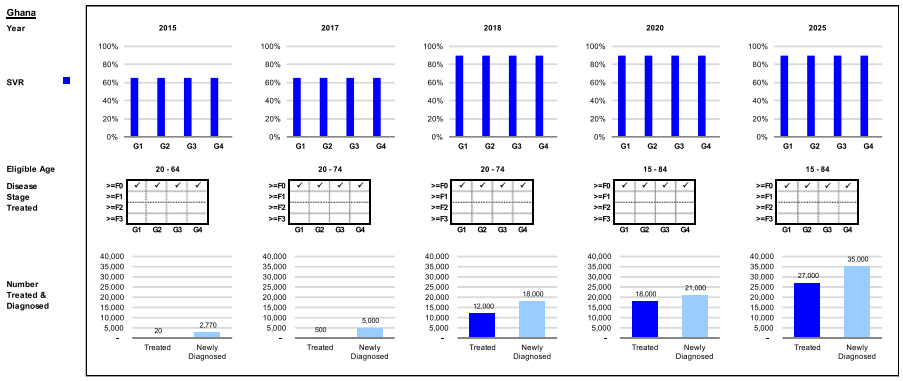

FIGURE 8 Ghana model inputs, by year

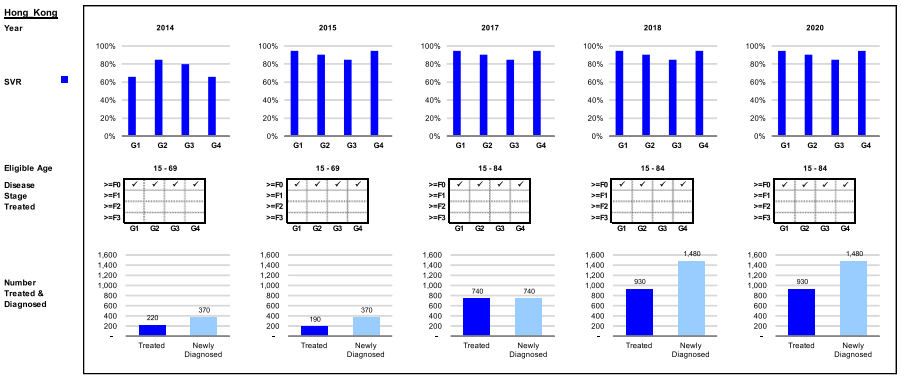

FIGURE 9 Hong Kong model inputs, by year

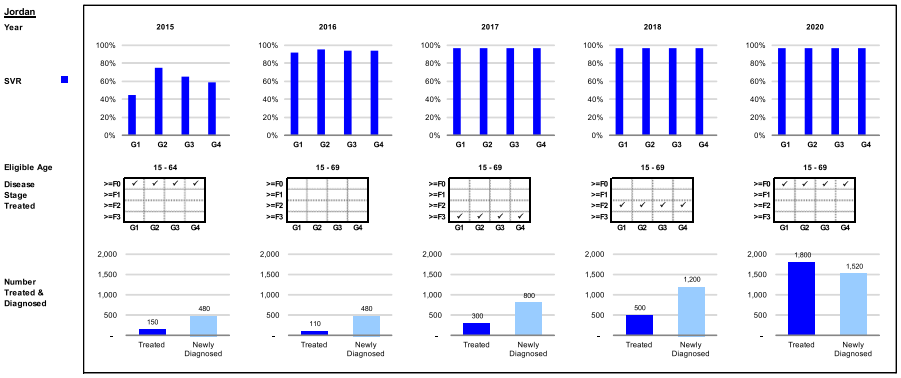

FIGURE 10 Jordan model inputs, by year

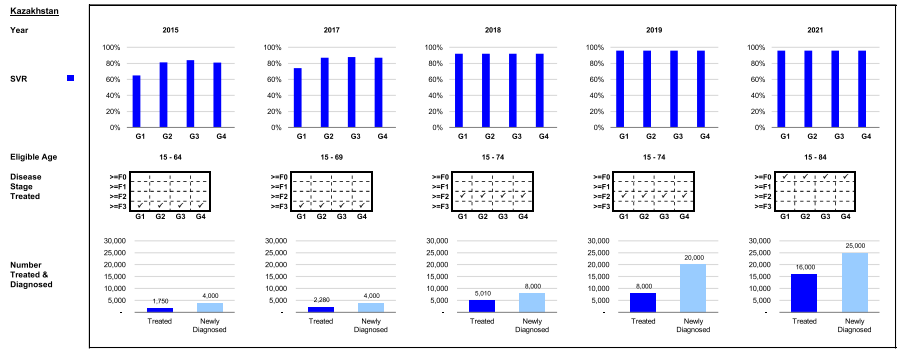

FIGURE 11 Kazakhstan model inputs, by year

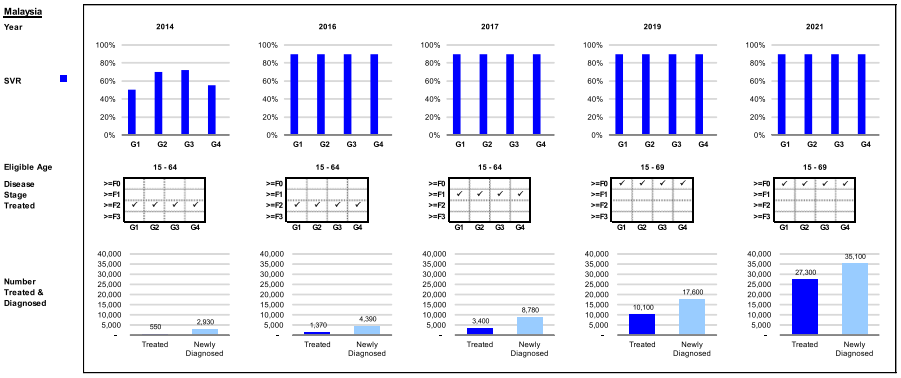

FIGURE 12 Malaysia model inputs, by year

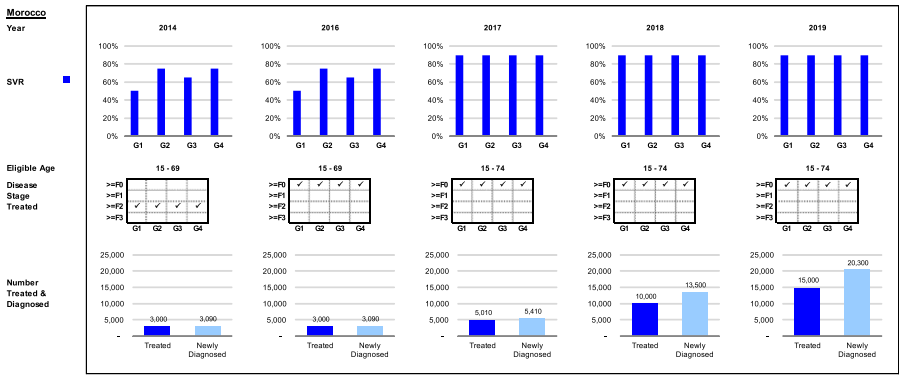

FIGURE 13 Morocco model inputs, by year

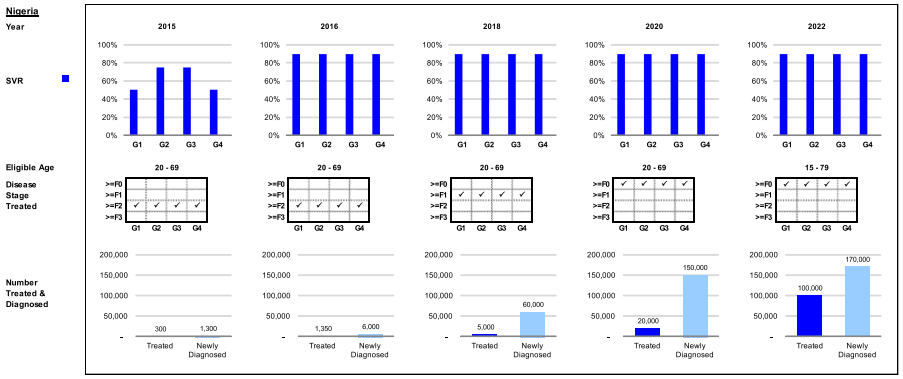

FIGURE 14 Nigeria model inputs, by year

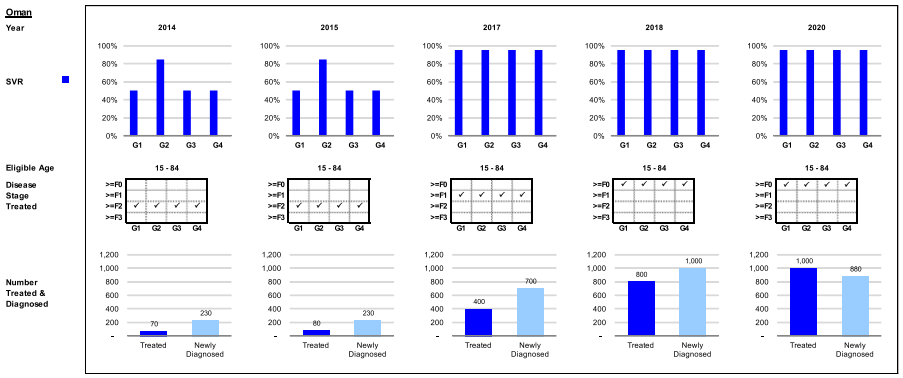

FIGURE 15 Oman model inputs, by year

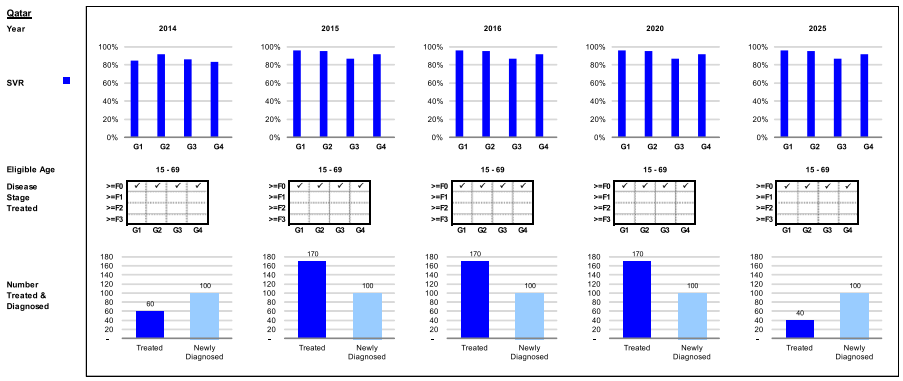

FIGURE 16 Qatar model inputs, by year

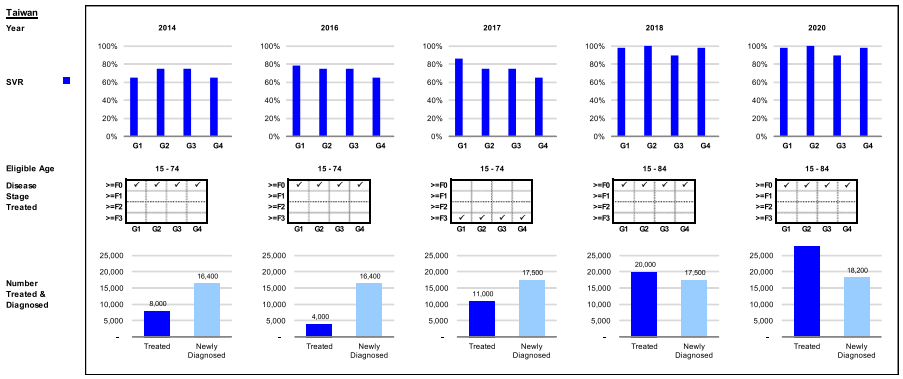

FIGURE 17 Taiwan model inputs, by year

FIGURE 18 Change in HCV morbidity and mortality, by scenario, 2015-2030

In all instances, viremic infections represented current HCV or chronic HCV infections. The term viremic was used throughout this study to highlight the presence of HCV virus. The term incidence was used for new HCV infections and not newly *diagnosed* infections. Hepatocellular carcinoma (HCC) referred to the total number of viremic HCV-related HCC cases, rather than new cases. Additionally, all reductions by disease stage were assumed to occur among the viremic HCV population, that is the effects of non-HCV-related liver disease were not considered in this analysis.

FIGURE 18 (Continued)

2.1 | Birth cohort effect

The age distribution of each country was gathered from published data and reported previously.[6] The disease progression model was used to age the HCV-infected population after taking into account mortality and SVR.[4] For this analysis, the median age in each 5-year age cohort was selected and converted to a birth year. A range of birth years was selected that accounted for approximately 70% (or more) of the total HCV-infected population using the 2015 HCV population distribution.[4]

3 | RESULTS

The results of the analyses are summarized in Figure 18. In meeting the WHO target of a 65% reduction in liver-related deaths, countries would also reduce cases of compensated and decompensated cirrhosis and HCC by 45%-85% by 2030. The birth cohort effect in the HCV-infected population is shown in Figure 19. Each bar represents the range of birth years, with the value on each bar showing the percentage of the total infected population who were born between the years shown. Country-specific scenario results are discussed below.

3.1 | Bahrain

An aggressive treatment and diagnosis strategy to achieve the WHO targets would result in 14 200 fewer viremic individuals in 2030, an 85% reduction as compared to 2015. Doing so would require the number annually treated to increase from 50 in 2015 to 1610 by 2025 and the number annually diagnosed to expand from 280 in 2015 to 1170 by 2025.

FIGURE 18 (Continued)

3.2 | Bulgaria

Achieving the WHO targets with an aggressive treatment strategy would result in 75 600 fewer viremic individuals in 2030, an 80% reduction as compared to 2015. Annual number treated would need to expand from 720 in 2015 to 6000 in 2025. An increase in annual number diagnosed would be required from 1200 in 2015 to 6100 in 2025. This scenario assumed an increase in average SVR to 95% with the adoption of DAAs in 2017.

3.3 | Cameroon

With an aggressive treatment strategy, there would be 122 000 fewer viremic individuals in 2030, a 75% reduction as compared to the 2015 base case. To reach the WHO targets, treatment would need to be expanded from fewer than 1000 patients treated in 2015 to 9500 by 2025. Similarly, the number of diagnosed patients would need to increase to 10 500 by 2025. This scenario incorporates the introduction of DAAs in 2016, which increased the average SVR to 90%.

3.4 | Colombia

Utilizing an aggressive treatment and diagnosis strategy, there would be a 95% reduction in the total number of viremic individuals, representing 364 000 fewer viremic individuals in 2030, relative to 2015. Achieving the WHO targets would require an increase in annual number treated from 1000 in 2015 to 33 600 by 2025 and the annual number diagnosed from 3190 in 2015 to 57 400 by 2025. An increase in SVR to 90% due to the adoption of DAAs in 2016 was assumed.

3.5 | Croatia

Utilizing an aggressive treatment and diagnosis strategy, there would be a 95% reduction in the total number of viremic individuals, representing 25 300 fewer viremic individuals in 2030, relative to 2015. To

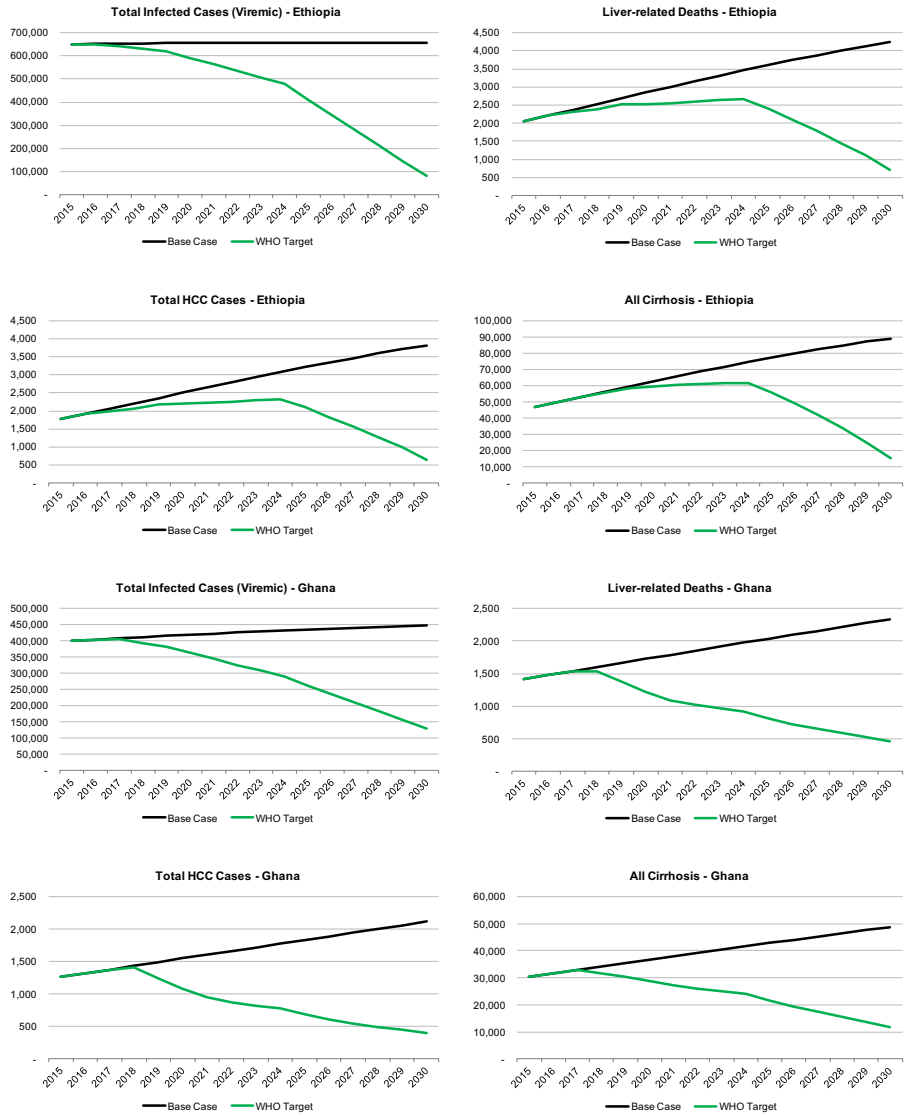

FIGURE 18 (Continued)

achieve the WHO targets, Croatia would need to increase the annual number treated from 150 in 2015 to 2970 by 2025 and the annual number diagnosed from 150 in 2015 to 2310 by 2025.

3.6 | Dominican Republic

If the WHO targets are met, there would be 63 200 fewer viremic individuals in 2030, a 90% reduction as compared to the base case. Reaching the WHO targets would require treatment to expand from 270 annually treated in 2015 to 7000 by 2025. Diagnosis would also need to expand from 690 cases diagnosed annually in 2015 to 6500 by 2025.

3.7 | Ethiopia

With treatment more than doubling annually, there would be 566 000 fewer viremic individuals in 2030, an 85% reduction from 2015. To achieve the WHO targets, an expansion of annual number treated would be required, from 2000 in 2015 to 65 000 by 2025. Number of cases annually diagnosed would also need to be increased from 1990 in 2015 to 49 700 in 2025.

3.8 | Ghana

With an aggressive treatment strategy, there would be 270 300 fewer viremic individuals in 2030, a 70% reduction compared to the base case. Achieving the WHO targets would require a treatment expansion from 20 annually treated in 2015 to almost 35 000 by 2025 and an increase in cases annually diagnosed from 2770 in 2015 to 35 000 in 2025. This scenario assumed an increase in SVR to 90% starting in 2015 due to the arrival of DAAs.

3.9 | Hong Kong

With an aggressive treatment and diagnosis strategy, there would be 13 500 fewer viremic individuals in 2030 than in 2015, a 90% reduction. This strategy would achieve the WHO targets by increasing the

FIGURE 18 (Continued)

annual number treated and diagnosed to 1000 and 1480 by 2025 and 2018, respectively.

3.10 | Jordan

With an aggressive treatment and diagnosis strategy, there would be 21 500 fewer viremic individuals in 2030, an 85% reduction as compared to 2015. Increasing the annual number treated to 1900 and the annual number diagnosed to 1570 by 2025 would result in meeting the WHO targets.

3.11 | Kazakhstan

With an aggressive treatment and diagnosis strategy, there would be 260 000 fewer viremic individuals in 2030, an 80% reduction as compared to 2015. Increasing annual number treated from 1750 in 2015 to 26 000 by 2023 would be required to achieve the WHO targets. The analysis also found that a scale-up of treatment would require an increase in annual number diagnosed (from 4000 to 25 000 by 2021) to avoid running out of patients to treat.

3.12 | Malaysia

With an aggressive treatment strategy, there would be 373 000 fewer viremic individuals in 2030, a 95% reduction as compared to the base case. This strategy would achieve the WHO targets by increasing the annual number treated and diagnosed to 41 000 and 35 100, respectively, by 2026.

3.13 | Morocco

With an aggressive treatment strategy, there would be 299 000 fewer viremic individuals in 2030, a 95% reduction as compared to 2015. Achieving the WHO targets would require a scale-up of number

FIGURE 18 (Continued)

annually treated from 3000 patients in 2015 to 33 100 patients by 2025. The analysis also found that a scale-up of treatment would require an increase in annual number diagnosed (from 3100 to 30 500 by 2025) to avoid running out of patients to treat.

3.14 | Nigeria

With an aggressive treatment strategy, there would be 1 804 000 fewer viremic individuals in 2030, a 70% reduction compared to the base case. To achieve the WHO targets, the number annually treated would need to increase from 300 in 2015 to 180 000 by 2030 and the number annually diagnosed from 1300 in 2015 to 195 000 by 2025. This scenario assumed an increase in SVR to 90% starting in 2016 with the arrival of DAAs.

3.15 | Oman

An aggressive treatment and diagnosis strategy would result in 13 600 fewer viremic individuals in 2030, an 85% reduction as compared to 2015. The estimated number of patients annually treated in 2015 would need to be increased to 1150 by 2025 (from 70 in 2015) in order to achieve the WHO targets. This scale-up of treatment would require an increase in annual number diagnosed from 230 in 2015 to 1000 by 2018 to avoid running out of patients to treat.

3.16 | Qatar

The current treatment paradigm in Qatar was projected to achieve the WHO target by 2030. There would be 1190 fewer viremic individuals in 2030, a 90% reduction as compared to 2015. There would be fewer than 600 total viremic cases by the year 2020.

3.17 | Taiwan

With an aggressive treatment and diagnosis strategy, there would be 440 000 fewer viremic individuals in 2030 than in 2015, an 85%

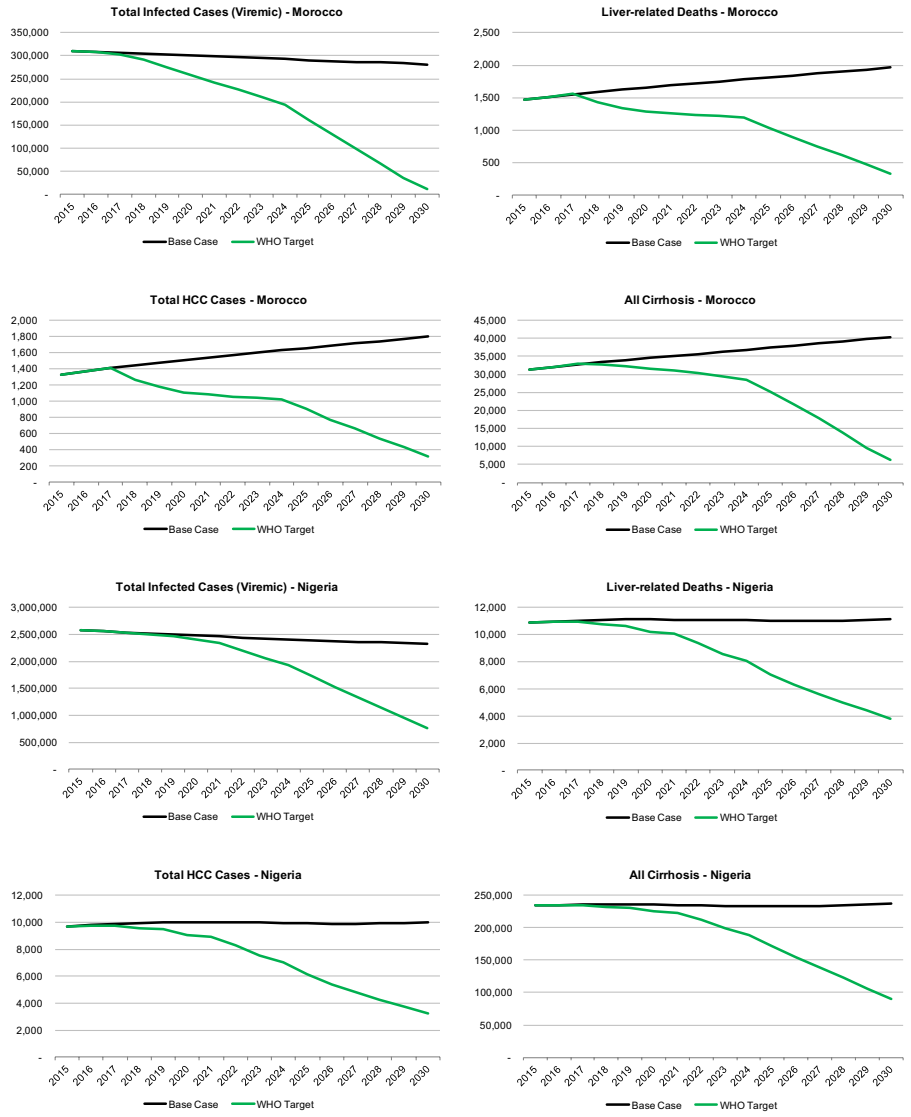

FIGURE 18 (Continued)

reduction. This strategy would achieve the WHO targets by increasing the annual number treated and diagnosed to 30 000 and 18 500, respectively, by 2025.

4 | DISCUSSION

With the introduction of highly efficacious therapies for HCV treatment, 2015 and 2016 were critical transition years for some countries, as health officials planned and began to implement new treatment strategies (ie, Hong Kong and Qatar). For other countries considered in this analysis, discussions are underway to make HCV treatment accessible in the future (ie, Ghana and Bulgaria). This analysis suggests that achieving WHO targets for the elimination of HCV is possible with a multifaceted approach that increases screening, expands treatment access to F1 and F0 patients and gradually scales up the number of treated patients annually.

Using today's treatment paradigm, HCV-related morbidity and mortality is expected to increase through 2030 in most countries, with the exception of Qatar and Taiwan.[1] Additionally, in four countries (Ethiopia, Ghana, Jordan and Oman) the total number of HCV-infected individuals is expected to increase.

As part of this analysis, a WHO target scenario was developed to meet the GHSS targets for 2030: a 65% reduction in HCV-related mortality, a 90% reduction in new cases and 90% of all cases receiving a diagnosis. In developing these scenarios, the future SVR as well as medical eligibility, age range and number treated and diagnosed annually were modified to achieve the desired reduction in mortality. The number diagnosed annually was further modified to achieve 90% diagnosed by 2030. The reduction in new infections was directly input into the scenarios. Therefore, it is assumed that factors both inside the scope of the model (eg, treatment expansion and reduction in total infection) and outside the scope of the model (prevention efforts such as education and needle programs) account for the reduction in new

FIGURE 18 (Continued)

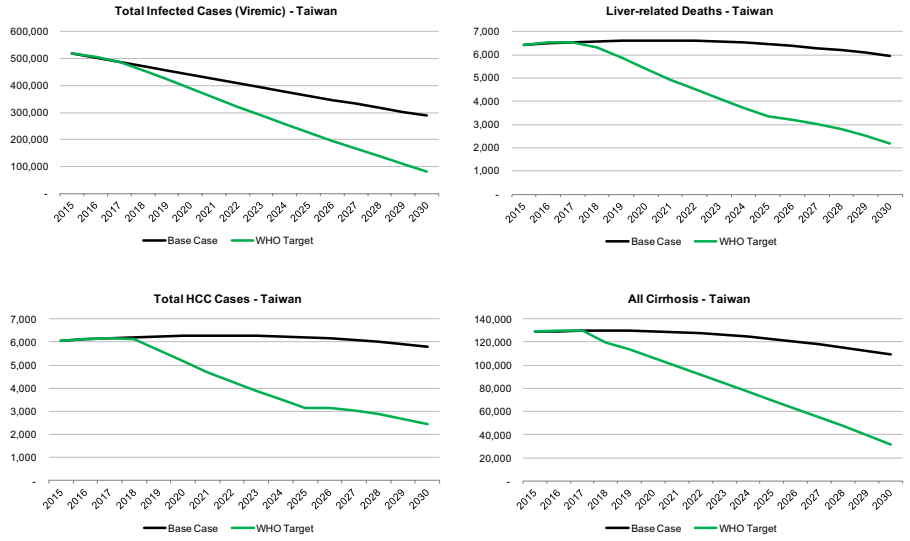

FIGURE 18 (Continued)

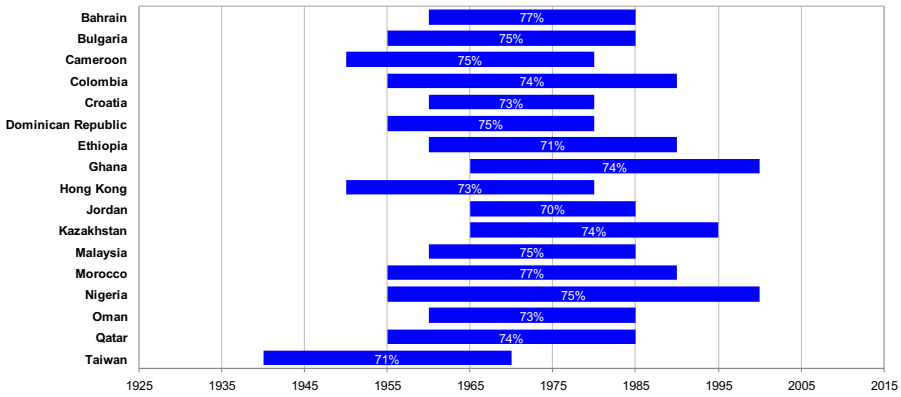

FIGURE 19 Distribution of HCV-infected population by birth year cohort

infections. The feasibility of achieving the WHO targets varies by country due to the heterogeneity in baseline disease projections over the next 15 years. For example, under the base case assumptions, liver-related mortality is projected to decline in a few countries while most other countries are projected to see increases in the number of deaths, some to a very large degree. Factors that influence this include the age of the infected population and the strength of the current treatment paradigm.

A key observation of this analysis was that increased treatment coverage and SVR in patients who were >F2 had the largest impact in reducing morbidity and mortality. However, treatment of F0-F1 patients was necessary to achieve reductions in total cases and prevent ongoing transmission. The WHO target scenarios were most effective when following a strategy of prioritizing treatment in >F2 patients in the first few years before expanding treatment to all. The exception was in countries where the number of diagnosed and treated patients was so low to begin with that there were too few patients diagnosed with advanced disease. This strategy did have a major drawback. The HCV-infected population is ageing, and not treating early-stage patients meant that patients would continue to advance to higher fibrosis stages, cirrhosis and HCC. Thus, the lower rates of advanced liver-related disease and mortality would not be sustained without additional intervention. Even in a scenario where all infections are aggressively targeted, the age of the infected population is one of the key variables for not being able to feasibly achieve zero infections in a country. Another challenge to achieving the WHO targets and/or complete eradication is immigration in today's mobile society. The models take into account the assumption that some new cases always entered the country through immigration. The long-term goals of the WHO targets will require a global effort to eliminate the virus across borders.

4.1 | Bahrain

Under the current treatment structure, the prevalence of chronic HCV is projected to decrease by 5% by 2030, which is relatively static given that new DAAs are already available. The estimated number of patients currently treated (50 annually) is low due to patients waiting on DAA therapies and the ramp up of DAA availability.

The strategy to achieve the WHO targets is most effective when treatment is restricted to more advanced patients (≥F3) in the first several years before expanding to all fibrosis stages and older patients. However, because 77% of all infections in Bahrain are among those aged 32-57 years, targeting this younger population would be more effective for diagnosing cases and reducing the overall infection rate.

4.2 | Bulgaria

Under the current treatment structure, in which an estimated 0.8% of the infected population receives treatment annually, the prevalence of chronic HCV was projected to decrease by 18%. An ageing infected population contributed to the projected decline in prevalence. Achieving the WHO targets, in addition to increasing treatment and diagnosis, would require an expansion of the treated population to include F1 and F0 cases and higher SVRs with the adoption of DAAs in 2017.

4.3 | Cameroon

In this analysis, it was found that the adoption of higher SVR therapies would have a small impact on the burden of advanced disease. These therapies will have to be combined with an aggressive treatment strategy to achieve a 75% reduction in total viremic infections.

The strategies modelled here required increases in the diagnosed population, as it was estimated that less than 10% of the viremic infected population was living with a diagnosis. This input has some uncertainty, however, as it was estimated through expert input in the absence of a national registry.

4.4 | Colombia

The HCV prevalence in Colombia is comparable to many countries in the Americas. Under the current treatment paradigm, HCV infections will decline by 20% by 2030. However, the most costly stages of the disease burden, including cirrhosis, decompensated cirrhosis and HCC, are expected to increase 45%-70%. Currently, Colombia allows the

treatment of all fibrosis stages, thus is in a unique position to save on screening costs.

To meet WHO 2030 targets, large increases in treatment, diagnosis and prevention would be necessary. However, 74% of all viremic individuals were born between 1953 and 1988 making targeted screening and treatment a feasible way to address the disease burden. By focusing on the older patients in this age cohort, there would be faster and larger decreases observed in the later stages of the disease and the WHO targets could be met more quickly.

4.5 | Croatia

Under the current treatment structure, the prevalence of chronic HCV was projected to decrease by 6000 patients, a 25% decline compared to 2015. A low incidence rate (4.5 per 100 000) and an ageing infected population contribute to the projected decline in prevalence. Achieving the WHO targets, in addition to increased number of cases treated and diagnosed, would require treatment to expand to F1 and F0 cases. It is assumed that Croatia will adopt new DAAs leading to a 90% average SVR for treatment in 2017.

4.6 | Dominican Republic

Under the current treatment structure, the prevalence of chronic HCV is projected to decrease by 15%, but advanced liver disease and liver-related mortality are projected to increase by 85%-100%. Large increases in treatment must be paired with increased diagnosis rates to reduce the disease burden. Additionally, to prevent new infections, treatment must eventually be expanded to F1 and F0 patients.

4.7 | Ethiopia

Under the current treatment structure, the prevalence of chronic HCV was projected to minimally increase. A low treatment rate (0.3%) contributes to the projected minimal change. In this analysis, it was found that the adoption of higher SVR therapies among patients with fibrosis (≥F1) would have no impact on the burden of advanced disease without increasing the number of patient treated.

Treatment in Ethiopia is limited; it was estimated that approximately 10 000 patients were treated over the course of 5 years. However, current therapies are expensive for many patients throughout the country, which is a barrier to increasing the number of patients treated in the future.

4.8 | Ghana

Under the current treatment structure, the prevalence of chronic HCV between 2015 and 2030 was projected to increase by 12%. The WHO target strategy modelled here required a sharp increase in the diagnosed population, as it was estimated that only 7% of the viremic infected population was living with a diagnosis. This input has some uncertainty, however, as it was estimated through expert consensus in the absence of a national registry.

4.9 | Hong Kong

Under the current treatment strategy, the number of viremic infections is expected to decline by 18% by 2030. However, advanced liver-related morbidity and mortality will continue to increase. This is likely explained by the older age distribution of the infected population; over half of all infections are among those older than 47 years. The higher rate of mortality in the older ages likely more than offsets the incidence of new infection. Modelling the increased use of high SVR therapies, however, showed an 80%-85% reduction in cases of cirrhosis, decompensated cirrhosis and HCC by 2030. It is important to note that focusing on targeting treatment in the older infected population would be imperative to the effectiveness of such an intervention.

4.10 | Jordan

Under the current treatment strategy, the number of viremic infections is expected to increase 7% by 2030 and then remain stable into the future. This is likely a result of a moderate incidence rate (8.3 per 100 k) that is partially offset by a treatment rate of 0.6%. Modelling the use of increased SVR therapies, however, showed a 65% reduction in cases of cirrhosis, decompensated cirrhosis and HCC. It is important to note that this intervention would be most effective when targeted screening at patients aged 32-57 years, as this group accounts for greater than 70% of all infections.

4.11 | Kazakhstan

Under the current treatment structure, the prevalence of chronic HCV is projected to remain relatively static, decreasing by 3% by 2030. Liver-related morbidity and mortality, however, were projected to increase by 60%-65% by 2030. Subsequently, the strategy to achieve the WHO targets is most effective when treatment is restricted to more advanced patients (≥F2) in the first several years and made available to older patients.

4.12 | Malaysia

Under the current treatment strategy, the number of viremic infections is expected to decline by 11% by 2030. However, advanced fibrosis and liver-related morbidity and mortality were projected to increase by 100% compared to 2015. While the overall prevalence will decline due to low incidence, those who are currently infected will continue to advance to liver-related morbidity. Modelling the increased use of high SVR therapies with expansion of treatment and diagnosis would thus be most effective when restricted to patients with F2 and higher fibrosis in the initial years.

4.13 | Morocco

Under the current treatment structure, the prevalence of chronic HCV was projected to slightly decrease by 9% from 2015 to 2030. However,

advanced liver-related morbidity and mortality were projected to increase at a higher rate (30%-35%) over that same time.

The strategy to achieve the WHO targets is thus most effective when treatment is restricted to more advanced patients (≥F2) at first and made available to older patients before expanding to all patients.

4.14 | Nigeria

Under the current treatment structure, the prevalence of chronic HCV was projected to decrease by 10% from 2015 to 2030. However, advanced liver-related morbidity and mortality were projected to increase by 1%-3% over that same time. The WHO target strategy modelled here required an increase in the diagnosed population, as it was estimated that just about 5% of the viremic infected population was living with a diagnosis. This input has some uncertainty, however, as it was estimated through expert input in the absence of a national registry.

4.15 | Oman

Under the current treatment structure, the prevalence of chronic HCV is projected to remain relatively static, increasing by only 3% by 2030. The strategy to achieve the WHO targets is most effective when treatment is restricted to more advanced patients (≥F2) in the first several years and made available to older patients before expanding treatment to all patient population segments. And because >70% of all infections in Oman are among those aged 32-57 years, targeting these younger patients for screening would more efficiently identify patients.

4.16 | Qatar

Under the current treatment strategy, the number of viremic infections is expected to greatly decrease by 2030, eventually leading to elimination. This is likely a result of a high treatment rate with new DAAs among nationals with HCV (13% in 2015). In fact, the current treatment and diagnosis rates were projected to achieve the WHO targets. It is important to note that nationals make up only a small percentage of the country's population and of the infected population in Qatar. Incidence will likely not drop in the national population even as most patients become cured. Interventions that target the immigrant population as well would be necessary to achieve the WHO targets across the total population.

4.17 | Taiwan

Under the current treatment strategy, the number of viremic infections is expected to decline by 45% by 2030. Advanced liver-related morbidity and mortality were also projected to show modest declines between 5%-17% compared to 2015. This is likely explained by the combination of the advanced age of the patient population (>70% between 42-72 years), the relatively high treatment rate (1.5% annually) and the relatively low incidence rate (13 new cases per 100 000 people). It is important to note that expanding treatment to the older ages was critical to achieving these targets. There is evidence showing that HCV infection may be associated with extra hepatic diseases[7,8] suggesting that the benefits of such a strategy may extend beyond the hepatic disease burden.

4.18 | Utility of HCV screening

As shown previously,[4,6] diagnosis remains low in many countries. In all countries except Qatar, the diagnosis rate was increased in future years in developing the WHO target scenarios in the models. This was required to both provide a sufficient patient pool for treatment as well as to achieve the WHO target of diagnosing 90% of all cases by 2030. However, it is not clear if the number of newly diagnosed patients can realistically be increased without a focused screening strategy and with the current medical infrastructure in each country.

One way to more efficiently identify cases, as recommended by the U.S. Centers for Disease Control and Prevention, is to screen the birth cohorts with a higher prevalence rate.[9-11] A birth cohort analysis was conducted for each country, and the results are shown in Figure 19. The analysis identified specific age ranges accounting for over 70% of the infected population. The cohort ranges in the countries analysed varied from 20 years (Croatia and Jordan) to 45 years (Nigeria), likely due to variations in risk factors. The ranges tended to be wider when nosocomial infection was identified as a risk factor (eg, blood transfusions from unscreened blood). In countries where IDU was identified as a key risk factor, the birth cohort range often skewed towards younger ages. Age distributions within each country's total populations might also account for some of the variation in the range and age of the birth cohorts. The birth year cohorts for these countries provide an efficient mechanism for identifying new patients as part of a national screening strategy.

4.19 | Limitations

There were several limitations of this study. SVR rates for current treatment protocols were often based on clinical data from centres highly adept at and experienced in treating patients and limiting adverse events. SVR rates observed outside of these ideal settings could be lower,[12] resulting in a greater need to increase annual treatment rates than what is reported here in order to achieve the WHO target scenarios. In addition, there is uncertainty around HCV prevalence estimates identified for each country.[4] Therefore, the required actions to achieve the WHO targets may be more or less pronounced if this analysis under- or over-estimated the true prevalence.

Another limitation was that increases in treatment rate, diagnosis rate, eligibility and SVR in developing the WHO target scenarios were assumed to be implemented immediately. In reality, the market entry of new therapies, adoption of policies and implementation of national disease management strategies would take several years to actualize. However, time sensitivity analyses examining the impact of accelerating or delaying initiating strategies consistently demonstrated that the WHO targets were more likely to be met and more efficiently achieved when the strategies were implemented sooner than later.

A final limitation of this analysis is that disease progression was considered to halt once patients were cured. In reality, it has been

shown that the risks for advancing to liver-related morbidity and mortality can persist even after achieving SVR, though at significantly lower rates.[13] Therefore, the model could underestimate the rate of increased treatment and diagnosis needed to achieve the WHO target of a 65% reduction in liver-related mortality. However, any underestimation is likely to be minimal, as the bulk of this reduction is due to the decrease in early-stage chronic infections, which are at very low risk of progressing to advanced liver disease once cured.

4.20 | Conclusion

This analysis showed that the total number of HCV infections is expected to decline or remain flat in the majority of countries if current disease management paradigms are maintained through 2030. Nevertheless, HCV-related morbidity and mortality are expected to significantly increase over the next 15 years in almost all countries. Achieving the WHO targets is most feasible when strategically active and targeted screening programs to find and identify HCV-infected individuals are combined with the scale-up and strategic use of high SVR therapies in the patient population.

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