

Global change in hepatitis C virus prevalence and cascade of care between 2015 and 2020: a modelling study

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Global Change in Hepatitis C Virus Prevalence and Cascade of Care between 2015 and 2020: A Modeling Study.

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Abbreviations: Global Burden of Disease (GBD); Hepatitis C Virus (HCV); Hepatocellular Carcinoma (HCC); Ribonucleic Acid (RNA); Uncertainty Intervals (UI); Sustained viral response (SVR); World Health Organization (WHO)

Abstract

Background: Since the release of the first global hepatitis elimination targets in 2016 and until the COVID-19 pandemic started in early 2020, many countries and territories were making progress toward hepatitis C virus (HCV) elimination. This study aimed to evaluate progress towards HCV elimination at the start of the year 2020, prior to the pandemic.

Methodology: This analysis includes a literature review, Delphi process and mathematical modeling to estimate HCV prevalence and cascade of care from 1/1/2015 to 12/31/2020. Epidemiological data were collected from published sources and grey literature and were validated with local experts. A Markov model was used to forecast prevalence and disease burden for countries with data. Model outcomes were extracted to calculate population-weighted regional averages, which were used for countries or territories without data. Finally, regional and global prevalence, cascade of care and disease burden estimates were calculated based on 235 countries/territories.

Findings: Models were built for 110 countries or territories: 83 approved by local experts, 27 based on published data alone. Using data from these models, plus population-weighted regional averages for countries/territories without models, a global prevalence of viremic HCV of 0.7% (95% UI: 0.7%–0.9%) [56.9 (55.2–67.8) million infections] on January 1, 2020 was estimated. This represents a decline of 6.8 million viremic infections (7.5 million incident infections, 5.5 million deaths, 8.8 million treated and cured) from an updated 2015 prevalence estimate of 63.7 (61.8–75.8) million infections. By the end of 2020, 12.9 million persons were living with a diagnosed viremic infection. In 2020, 0.6 million patients were started on treatment.

Interpretation: In 2020, there were an estimated 56.9 million viremic infections globally. Although this represents a decline from 2015, our forecasts suggest we are not currently on track to achieve global elimination targets. As countries recover from COVID-19, this work can help re-focus efforts aimed at HCV elimination.

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Keywords: Hepatitis C, global, prevalence, cascade of care, hepatocellular carcinoma, cirrhosis, World Health Organization

Research in context**Evidence before this study**

Over the last decade, there have been a number of global estimates of hepatitis C virus (HCV) prevalence published by this group including global prevalence assessments (published in 2014, and 2016); pediatric prevalence (2020) and prevalence among women of childbearing age (2021). The World Health Organization has also published reports on global prevalence, incidence and mortality associated with HCV (2017, 2021). Global analyses of HCV-related cancer and mortality have been undertaken by the Institute for Health Metrics and Evaluation and the International Agency for Research on Cancer. Finally, estimates of HCV incidence, and incidence among key populations including people who inject drugs, have been published by the University of Bristol and UNSW Sydney. In addition to searching institutional websites for recent publications from the aforementioned groups, we identified global studies during our country/territory-level literature search of PubMed and grey literature. The following search terms ("Hepatitis C" AND "Prevalence" AND "Country/Territory") were used to identify articles in all languages published between April 1, 2016, and March 31, 2021, that build upon our previous work.

Added value of this study

Building on our 2016 estimate of the global prevalence of HCV, this study provides a progress update for 2020, along with a revised 2015 baseline incorporating updated serosurvey results from large countries including Egypt, Brazil, Nigeria and the Democratic Republic of Congo (among others). Additionally, we report the HCV cascade of care as well as modeled outcomes and forecasts for the global burden of HCV – including measures of incidence and mortality. Our results were obtained from a literature search and the use of 110 country- or territory-specific disease burden models. To strengthen the analysis, more than 300 experts were consulted to validate the model inputs and outcomes. This led to 83 approved country/territory models, plus another 27 models that were developed based on published data alone. Additionally, we collected 2020 treatment data from 31 countries, allowing for preliminary forecasts of HCV disease burden in the years following the COVID-19 pandemic.

Implications of all the available evidence

At the beginning of 2020, there were an estimated 56.9 million viremic infections globally. Although this represents a decline from 2015, our forecasts suggest we are not currently on track to achieve global elimination targets. Of the ~56.9 million people infected with HCV in 2020, less than a quarter had been diagnosed, and only 600,000 were estimated to initiate treatment in that year. Of the more than 10 million persons initiated on DAAs between 2015 and the end of 2020, more than a third were in Egypt. With 10 years remaining in the fight to eliminate hepatitis as a public health threat, significant effort is still needed to eliminate hepatitis C virus. As decision makers evaluate their HCV elimination efforts and progress following the COVID-19 pandemic, this study provides an updated baseline for future activities.

Introduction

Hepatitis C virus (HCV) is a bloodborne virus with the potential to cause liver fibrosis, hepatocellular carcinoma (HCC) and liver-related deaths. Currently, there is no protective vaccine available, but the advent of direct acting antiviral (DAA) therapies that achieve sustained viral response (SVR) in >95% of people has drastically improved HCV management, even in patients with cirrhosis. Diagnosis of HCV is also improving with the increased availability of point of care diagnostics, including confirmatory tests for HCV ribonucleic acid (HCV RNA). Additionally, strategies to prevent contact with infected blood and blood products as well as blood-contaminated objects can effectively control the transmission of HCV.¹ Since no efficient HCV vaccine regimen is available,² HCV treatment and prevention of new infections remain the key measures for HCV elimination. However, if strategies are developed and implemented to both prevent new infections and effectively treat HCV cases (through efficient diagnosis/early detection of patients, and timely linkage to medical care and treatment) HCV can be eliminated as a public health threat.³

In 2016, the 69th World Health Assembly passed a resolution to eliminate viral hepatitis as a public health threat by 2030,⁴ and the World Health Organization (WHO) introduced global targets (65% reduction in mortality, 80% reduction in incidence, $\geq 90\%$ diagnosed, $\geq 80\%$ treated) for the care and management of HCV.⁵ In June 2021, interim guidance for country validation of viral hepatitis elimination was released, with the inclusion of new absolute targets (annual incidence ≤ 5 per 100,000 and annual mortality ≤ 2 per 100,000).⁶ The Center for Disease Analysis and the Polaris Observatory have been evaluating the global prevalence of HCV for almost a decade. Our first estimate, published in 2014, quantified viremic infections globally based on indexed and non-indexed (e.g., government reports) data published between 2000 and 2013.⁷ This analysis was novel in its estimation of viremic infections (HCV RNA-positive) rather than serological evidence of past or present infection (anti-HCV-positive).⁸⁻¹⁰ The second analysis, published in 2016, was expanded and strengthened through the use of disease burden modeling, through which we developed consistent, 2015 year-end prevalence estimates at an expanded scope (country/territory, regional, and global). The literature search was also extended through March 31, 2016.¹¹ Prevalence estimates from this publication were selected as the baseline for the WHO's Global Hepatitis Report 2017,¹ and served as a starting point for many countries or territories HCV elimination efforts.

The objective of this analysis was to evaluate national, regional, and global progress towards HCV elimination at the start of 2020. This time point was selected because it serves as both a reset point for countries/territories which may have deferred their HCV elimination efforts amidst the current crisis of the COVID-19 pandemic, and an assessment of HCV elimination progress five years after the approval and adoption of DAAs for clinical use. Furthermore, this analysis evaluates the cascade of care (viremic infections, diagnosed, treated, cured) at the Global Burden of Disease (GBD) Region and global level, based on available country/territory data through 2020.

Methods

This analysis integrates a literature review, a Delphi process, and modeling to estimate HCV prevalence and the cascade of HCV care among persons of all ages [age 0 (newborn) and older]. Empirical and programmatic data reflecting calendar year (January 1 through December 31) 2020 were retrieved and entered into the models. Model stocks (including prevalence, previously diagnosed) were summarized as beginning-of-year (January 1) outputs, while model flows (including incidence and disease progression) were summarized for the calendar year. Data were extracted for 2015 to serve as a revised baseline for the evaluation of HCV elimination progress, with 2020 data extracted to develop an annual, complete-year cascade of HCV care. Beginning-of-year 2020 data were extracted to generate an updated prevalence estimate for countries/territories. After extracting model data for countries/territories with models, population-weighted regional averages were calculated by GBD region. These regional averages were then applied for countries/territories without sufficient data to generate a model, in order to calculate regional and global estimates inclusive of 235 countries/territories. Prevalence estimates were described at the national, regional, and global levels, with the cascade of care described regionally and globally. The details of the data collection, scoring of data sources, Delphi process, and mathematical modeling are described briefly below and, in the appendix p4-20.

Country/Territory-level data collection and selection criteria

To evaluate HCV prevalence (including the diagnosed and undiagnosed population), a literature search of PubMed and non-indexed reports was performed to identify studies published between April 1, 2016, and March 31, 2021 (appendix p15). The outcomes of this search were combined with the outcomes of our previous analysis (encompassing studies published from January 1, 2000 – March 31, 2016). Non-indexed government reports, personal communication with country/territory experts, and additional studies identified through manual searches of references noted in publications were included when better data

were not available. The scope of the analysis included all countries/territories with a population of more than 1.5 million people, with *ad hoc* inclusions of nine countries/territories with smaller populations. These nine countries/territories were included following a request from country collaborators, ministries of health, or the WHO. Articles were scored using a multi-objective decision-analysis approach based on how well the prevalence estimate could be extrapolated to the general population (including population sampled, geographic scope and sampling procedure), the study sample size, and the year of analysis.^{7,11}

To estimate the population diagnosed with HCV, data were collected from (in order of priority) national notification or registry data, peer-reviewed literature, and expert opinion. When notification or registry data were used, the case definition was consulted to determine if notifications reflected anti-HCV, HCV RNA, or both. When necessary, the spontaneous clearance rate (based on previous publications surrounding the natural history of HCV) or country-provided viremic rate was used to adjust notified cases to estimate HCV RNA-positive annual diagnosed cases. In countries/territories where HCV was a notifiable infection and a reliable number of newly diagnosed cases was reported annually (including deduplication to ensure each patient was only reported once), the total number of diagnosed cases could be calculated by summing annual viremic diagnosed cases and subtracting mortality and cures.

The number of individuals treated annually through the end of 2020 was estimated from (in order of priority) national databases, audit sales data, government reports, estimates from major treatment centers, and drug suppliers. The scope of the population treated was collected to ensure that the final estimate for treatment reflected both the private and public markets. When treatment data were provided for a portion of the market, data were adjusted in discussions with the expert panel to capture sales or treatments in channels not reflected in the drug sales data or national database (appendix p33).

Similar to the prior analysis, a Delphi process was used to gain country/territory expert consensus and validate collected data to use as model inputs (*approved* country/territory data) (appendix p19-20).¹¹ Experts were identified through HCV-related scientific contributions, or through referrals and recommendations from leading researchers or WHO regional offices. In countries/territories where an analysis had not previously been conducted, two or more meetings were held to achieve consensus around input and output variables, and to validate the outputs against available empirical data. Country/territory models that were approved in the prior analysis were revisited for new data, and discussions were held with country experts to verify the inclusion of any novel prevalence studies.

For countries/territories where meetings with local experts could not be scheduled, published estimates were used (*estimated* country/territory data). Two epidemiologists reviewed and scored all published studies according to the methodology described above, and the highest-scored studies used for modeling. When inputs other than prevalence rate were unavailable for a country/territory, the population-weighted regional average (calculated using countries/territories within the same GBD Region) was used.

Country/Territory-level HCV disease burden modeling

After reviewing and scoring available studies, a Microsoft Excel[®]-based (version 365) Markov model of HCV infection, described previously,¹²⁻¹⁴ was populated with the highest-scoring epidemiological data for the country/territory of interest (appendix p16-18). The highest scoring prevalence study was selected as the base value for modeling, while other studies were used to estimate the high and low (including blood donor data) values for uncertainty analysis. Next, the model was used to forecast the total HCV prevalence (including the undiagnosed population) forward from the year of report to the beginning of 2020, accounting for annual incidence, mortality, and cure. From a methodological perspective, the biggest difference between the present and previous analysis¹¹ is the calculation of incidence: first, the incident HCV infections were partitioned into vertically and horizontally acquired infections. Second, both vertically and horizontally acquired infections were calculated as a function of prevalence of chronic HCV infections (among women of childbearing age for vertically acquired infections) in a dynamic model. The change in horizontally acquired infections was calculated dynamically, whereby the annual rate of change in incidence followed the rate of change in prevalence. Previously, HCV incidence was assumed to remain constant after the last year of data. As a result, a falling HCV prevalence due to treatment expansion leads to a reduction in incidence in the updated model. On the other hand, although the model does not consider populations susceptible to HCV infection partitioned by risk group, it implicitly allows for re-infection, whereby a rising HCV prevalence leads to an increased incidence. The changes to incidence forecasting were applied to 2020 estimates as well as the revised 2015 estimates and are discussed in greater detail in the appendix p12.

Within the model, the number of diagnosed (viremic) infections was calculated annually for the beginning of the calendar year, accounting for disease progression and mortality within the diagnosed population, as well as cures and newly diagnosed cases/infections over the course of the previous year. For this analysis, the number of persons ever diagnosed with HCV was also calculated separately using the number of total

viremic cases diagnosed in 2015 plus all newly diagnosed viremic cases from 2015 through 2020 — without accounting for mortality or cure.

After the last year of available treatment data, forecasts for future treatment starts were developed as follows: the default forecast approximated a logarithmic decline from the year of peak treatment in each country/territory to 50% of the peak treatment level over the course of five years (appendix p6). After five years, the number of patients treated annually was assumed to stay constant, unless better data were available to inform forecasts. This forecast was initially developed considering the trajectory of treatment initiations following the launch of pegylated-interferon (Peg-IFN) (unpublished data) and was later validated following the launch of DAAs (appendix p6). When country/territory-specific data were available to inform forecasts, those were used.

Global and Regional Estimates and Sensitivity Analysis

GBD regional population-weighted averages from approved and estimated models were calculated and applied for countries/territories with missing data to estimate the global HCV prevalence, cascade of care and disease burden. The uncertainty in prevalence for approved and estimated models was used to model the prevalence uncertainty at GBD regional level which were then applied to countries with missing data. Six countries/territories with approved or estimated models (Australia, Egypt, Georgia, India, Mongolia, and Pakistan) were excluded from initial calculations (but were included in final summaries at a regional and global level) because their underlying epidemic or interventions were not representative of those seen in neighboring countries/territories. Countries/territories without a formal GBD designation were assigned an imputed GBD Region (appendix p 21). After applying the GBD regional averages for countries without data, data were summarized for 235 countries/territories by GBD region, WHO region, World Bank (WB) income groups, and/or globally.

Sensitivity analysis was conducted using Crystal Ball® (Release 11.1.3708.0), an Excel® add-in by Oracle®. This software allows us to use customized distributions to capture the uncertainty for any given variable. It then changes one input variable at a time and records the impact of each input variable on the desired forecast (outcome) variable (in this case the 2020 global viremic prevalence). Finally, the software ranks inputs by their impact on the forecast variable. Probability distributions¹⁵ used for key inputs have been described previously.¹¹ Monte Carlo simulation was used to estimate 95% uncertainty intervals (UI). To calculate regional and global uncertainty ranges, two sources of uncertainty were considered — country/territory-level uncertainty in prevalence (based on literature search results and expert panel

discussions) and the contribution of each country/territory to regional/global prevalence. The 2020 country/territory prevalence estimates and 95% UIs were consolidated and defined as assumption variables. Sensitivity analysis was run to identify countries/territories that accounted for the greatest variation in global prevalence through their estimated prevalence range and inclusion in regional averages. Due to the scarcity of low/high ranges around the collected (largely empirical) diagnosis and treatment data, uncertainty in these inputs could not be modeled. Given the limitations of these input data, we applied the uncertainty in prevalence to regional and global cascades of care.

Role of the funding source

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Results

Data collection identified 7,881 studies through PubMed with a publication date between April 1, 2016, and March 31, 2021. When combined with prevalence studies published prior to 2016^{7,11} and expert input, prevalence estimates were available for 115 countries/territories, accounting for 93% of the world's population. Treatment data were available for 110 countries/territories while diagnosis data, including annually diagnosed and total previously diagnosed, were available for 93 and 87 countries/territories, respectively. Among countries reporting treatment data, data were obtained from (categories are not mutually exclusive) drug sales (including generics) data (39%), expert consensus (27%), national databases (26%) and published studies (8%). Among countries with diagnosis data, previously diagnosed estimates were obtained from expert consensus (45%), published studies (33%) and national surveillance or blood donor databases (22%). Estimates of annual diagnosed were from national surveillance or blood donor databases (42%), expert consensus (41%), and published studies (16%).

Models were built for 110 countries/territories that had (at minimum) data on HCV prevalence by age and sex. The inputs and outputs for 83 models were *approved* by country/territory experts and 27 were *estimated* using published data alone. This represents the addition of 12 new countries/territories that were previously not included as *approved* or *estimated*, and the validation of 16 country/territory models that were previously *estimated* and are now *approved* (appendix p18). The remaining countries/territories had insufficient data to create a model. Treatment data were available for 15 countries/territories that had insufficient data to create a model, representing 5% of the world's population, but less than 1% of HCV treatments from 2015 to 2019.

The evolution of the analysis is shown in Figure 1. The quality score of input prevalence data for *approved* or *estimated* countries/territories (1 being lowest quality, 3 being highest quality) is shown in the appendix, p34. The 2020 viremic HCV prevalence (percent and number) of the same countries/territories is shown in Figure 1A, while the prevalence of all countries/territories, including those with an extrapolated prevalence, is shown in Figure 1B. Lastly, the number of viremic infections for all countries/territories is shown in Figure 1C.

The numerical prevalence and total infections in 2015 and 2020 for *approved* and *estimated* countries/territories are shown in Table 1. The model input data for prevalence, quality score, year of prevalence estimate, uncertainty range, viremic rate, source of prevalence age distribution, and all corresponding references are included by country/territory in the appendix p22-27. Input data, by country/territory for previously diagnosed and newly diagnosed, annual treated and all corresponding references are included in the appendix p28-33.

The global prevalence of viremic (HCV RNA+) HCV infection was estimated to be 0.7% (95% UI: 0.7%–0.9%) at the beginning of 2020, corresponding to 56.9 (55.2–67.8) million viremic infections. This represents a reduction of 6.8 million viremic infections from a revised 2015 (beginning of year) estimate of 63.7 (61.8–75.8) million viremic infections [0.9% (0.8%–1.0%) prevalence]. The change in viremic infections resulted from the addition of 7.5 (7.3 – 8.9) million new chronic infections, the subtraction of 8.8 (8.5 – 10.4) million cured infections and the subtraction of 5.5 (5.3 – 6.5) million deaths (both all cause and liver related) from 2015 through the end of 2019 (Figure 2a). The progression of viremic infections from 2015 to 2020 among the 20 countries/territories with the largest number of viremic infections is shown in Figure 2b. Most notably, Egypt's national treatment program treated almost 3.5 million people from 2015-2019, moving them from 5th most infections globally in 2015 to 17th by 2020.

The cascade of care was estimated in two ways (Figure 3). First, a cumulative cascade was calculated relative to the 2015 baseline, which showed 33% (21.1 million) of the viremic population in 2015 (63.6 million) had ever received a diagnosis ever diagnosed (Figure 3), with 9.5 million people cumulatively initiated on treatment (45% of 21.1 million diagnosed) between 2015 and 2019 (Figure 4, appendix p35). The annual cascade for 2020 considered only persons who were still HCV RNA positive (i.e., adding chronic incident cases, and removing cured and mortality from both the prevalent and diagnosed segment). In 2020, an estimated 23% (12.9 million) of the viremic HCV population (56.8 million) was diagnosed and living with a viremic infection; and only 1.1% of prevalent cases were initiated on treatment in 2020 (641,000 treated out of 56.8 million viremic) (Table 2). The total number of treated patients was 10.5 million from 2015 through the end of 2020.

Regional estimates for 2020 HCV prevalence and cascade of care are shown in Table 2. In 2020, prevalence among GBD regions was highest in Europe, Eastern [2.9% (2.3%-3.2%)] and Asia, Central [2.6% (2.4%-2.8%)] while Asia, South [14.5 (13.2-24.2) million] and Asia, East [10.0 (8.6-11.9) million] had the largest numbers of viremic infections. The number of viremic infections remained constant or decreased between 2015 and 2020 in all regions, with the exception of Sub-Saharan Africa, East. In 2020, as in 2015, most viremic infections were concentrated in lower-middle income [26.0 (19.0-46.7) million] and upper-middle income countries [19.8 (14.4-24.8) million].

Based on annual treatment trends, over 1 million persons were expected to initiate treatment in 2020 (Figure 5a). Empirical treatment data for the year 2020 were available for 31 countries/territories. In countries/territories reporting 2020 data, the number of treated patients decreased 44% (mean) relative to 2019 (376,000 treated in 2020 compared with 675,00 treated in 2019). Of note, in 2020, Rwanda's screening and treatment campaign resulted in a more than a 20-times increase in the number of treatments, relative to 2019. Removing Rwanda from the calculation would suggest a 47% decline in the number of treated, globally in 2020 (360,000 treated in 2020 compared with 674,000 treated in 2019). Global treatment declines in 2020 were not only experienced as a result of the COVID-19 pandemic. In 2019, Egypt treated 1.9 million patients in the height of their elimination program, and future treatment numbers were expected to be markedly lower in the coming years following this success (Figure 5a).

Based on empirical data and future treatment forecasts, the annual number of new (incident) chronic infections was expected to remain relatively constant (2% decline from 1.43 million in 2020 to 1.40 million 2030) with an average of 1.42 million new infections expected each year through 2030 (Figure

5b). By 2030, end stage outcomes including liver deaths, hepatocellular carcinoma (HCC) and decompensated cirrhosis were expected to increase by 14-17% relative to 2020 (257,000 liver deaths in 2020 to 290,000 in 2030; 190,000 incident HCC in 2020 to 220,000 in 2030; and 148,000 incident decompensated cirrhosis in 2020 to 174,000 in 2030) (Figure 5b).

The top ten sources contributing the most to the global prevalence range (as per the sensitivity analysis) are shown in appendix p36. The top ten uncertainties listed account for more than 95% of the total variance in global prevalence.

The comparison of this and previous analyses is shown in appendix p37. Improvements in the quality [scale of 1 (lowest) to 3 (highest)] and availability of data have been observed since our last analysis, with the addition of high-quality estimates in countries/territories where data were previously unavailable, including Armenia (score = 2), Bhutan (score = 3), the Democratic Republic of the Congo (score = 2), Kyrgyzstan (score = 2), Rwanda (score = 3), and Tanzania (score = 3). Additionally, countries/territories are engaging in high-quality screening programs and serosurveys, to monitor progress [e.g., Egypt (score = 3)], or update older, lower-quality estimates, [e.g., Viet Nam (score = 3, previous score = 1)].

Discussion

The 2020 global prevalence estimate of 0.7% (0.7%–0.9%) or 56.9 (55.2–67.8) million infections is lower than estimates from previous years.⁹⁻¹¹ This is primarily due to two factors — the first being newer published serosurveys that resulted in a reassessment of the baseline 2015 prevalence estimate. The uncertainty intervals captured uncertainties in country/territory-level prevalence estimates on the overall forecasts. In total, 39 countries/territories had a new model or study that resulted in the country/territory level 2015 prevalence estimate deviating +/-20% from the prior analysis. Most notably, we were able to develop a new model for the Democratic Republic of the Congo (DRC) using data from a large-scale dried blood spot survey.¹⁶ This survey tested for HCV RNA and found a viremic prevalence of 0.9%,¹⁶ which resulted in a lower number of infections than our previous estimate based on the regional average (2.1%).¹¹ Additionally, relative to our previous study, more than 1 million fewer viremic infections in 2015 were estimated from both Egypt and Brazil, where new prevalence studies were available. Overall, our new 2015 prevalence estimate [0.9% (0.8%–1.0%)] is still within range of our original estimate published in 2016 [1.0% (0.8%–1.1%)].¹¹ However, it should be noted that the current estimate represents beginning of year 2015, while the initial analysis reflected end of year 2015.¹¹

The second factor contributing to a lower 2020 prevalence than previous estimates is the cumulative impact of time (aging, all-cause- and liver-related deaths, and incident infections) as well as treatment. The Markov model forecasts 2020 prevalence with annual adjustment for incidence, mortality, and cure. Between 2015 [63.7 (61.8–75.8) million viremic infections] and 2020 [56.9 (55.2–67.8) million viremic infections], we estimated there were 7.5 (7.3 – 8.9) million new chronic infections, 5.5 (5.3 – 6.5) million deaths (both all cause and liver related) and 8.8 (8.5 – 10.4) million cured infections (Figure 2a). The ability to present 2020 prevalence (including estimates of the undiagnosed population) and cascade of care alongside revised 2015 baseline estimates reflects the utility of modeling in elimination monitoring activities.

Our results are in line with the recent WHO's *Global progress report on HIV, viral hepatitis and sexually transmitted infections, 2021*¹⁷ although there are some notable differences in the analyses and outcomes. Data for the WHO global progress report was collected through a series of activities, that included sharing CDAF and other partner data from 2019 with countries/territories as a reference point for their global reporting activities. Countries/territories then chose to either keep the data or replace with their own estimates. In the event that the data available to and reported by national programs reflected only part of the story (i.e., older data were reported because newer data were not available; data were reported from the public sector but excluded efforts from the private sector; etc.), WHO could only report what had been provided or endorsed by countries. While many of the underlying data sources overlap with our analysis, the main difference in outcomes was that the CDAF team worked with local experts to determine the appropriate way to adjust sub-national data to the national level, and then model forward the results to the latest year (in this case 2020). The Delphi process and engagement of expert panels with a range of stakeholders represents a strength of our analysis. CDAF facilitators are trained to identify and challenge cognitive and motivational biases, including in situations where ministry of health is either not familiar with the data or would anchor to specific studies. Delphi process allows us to engage a range of national stakeholders and experts (from MOH and from outside of MOH) to provide balanced feedback and challenge one another's assumptions. As a result, the outcomes of the two analyses are complementary, but not identical.

Of the more than 10 million persons initiated on DAAs between 2015 and the end of 2020, more than a third were in Egypt. As a result of this monumental effort to screen and treat the entire population, Egypt's rank in the list of countries/territories with the largest number of viremic infections fell from fifth in 2015 to 17th by 2020. This effort is expected to reduce not only the number of HCC cases and liver related

deaths in the country but also the cost associated with managing HCV in the future.¹⁸ Globally, the number of patients initiated on treatment declined in 2020 relative to 2019; the cause of this decline is likely multifactorial. First, the Egyptian program has nearly concluded,¹⁸ thus reducing Egypt's relative contribution to global treatment efforts after 2019. Additionally, in many settings, previously diagnosed patients under care have already received treatment. Treatment efforts in special populations (including incarcerated populations or people who use drugs) vary substantially by country, with many countries still enforcing sobriety restrictions.¹⁹ Efforts to move beyond patients already diagnosed and under care may be stymied as many countries lack general population screening programs that could allow the number of treated patients to be maintained in the future. Although disease notification systems and patient registries exist in a number of countries, they are not universally reliable for estimating the number of people currently diagnosed and in need of treatment. Many countries with high-quality patient registries are finding that only 20-30% of diagnosed cases have been treated, indicating that linkage to care remains a bottleneck. As a result, current outreach efforts to test and link to care undiagnosed patients and patients lost to follow-up, especially among vulnerable populations, have not been sufficient to maintain the annual number treated. Additionally, the COVID-19 pandemic impacted logistics and distribution systems as well as access to health care and hepatitis screening and treatment services. Some countries reported stable treatment figures in 2020, but steep declines in new diagnoses. This may signal a problem for future elimination efforts. The overall impact of the pandemic is uncertain and will depend on the strength of current and future hepatitis elimination programs as well as the future impact of COVID-19, especially in light of COVID-19 vaccination efforts with substantial variations in vaccine availability.

To monitor progress toward the 2020 and 2030 elimination goals, and to guide future efforts in elimination planning, the cascade of care is presented in two formats (cumulative¹ and annual²⁰). The cumulative 2015-2019 cascade of care compares 'ever diagnosed' and 'ever treated' against a baseline of viremic prevalence in 2015, providing an easy visual for progress toward the 2020 and 2030 targets. However, since the true number of viremic infections changes each year with the addition of new infections and the subtraction of mortality and cured (unlike other diseases such as HIV or HBV without curative therapies), this cascade format may hide a growing viremic population, and is less useful for understanding the current needs in a country/territory or region. The annual cascade of care provides a snapshot of current progress and future needs but does not fully appreciate previous efforts. A great example of the different insights gleaned from the two cascades is seen in Figure 3c for lower-middle income countries/territories. Through the end of 2019, 21.1 million (28%) of the 63.7 million infected population was ever diagnosed, and 9.5

million (70%) of 21·1 million ever diagnosed patients were initiated on treatment. However, because 95% of patients initiated on treatment are cured of their HCV (and HCV must first be diagnosed before it can be cured), the annual cascade reflects that only 12·9 million (14%) of 56·9 million infections remaining in 2020 are living with a diagnosis. Focusing only on cumulative efforts misses the fact that the majority of the currently infected population remains undiagnosed. Similarly, focusing on cumulative treated may obscure annual declines in treatment. As countries evaluate their progress toward elimination, it will be important that they not only monitor cumulative past efforts but also maintain an annual snapshot of the cascade to highlight current gaps.

Our study has some limitations, many of which have been discussed previously. The availability and quality of data continue to limit the accuracy of forecasts. The inclusion of ranges addresses the uncertainty in the available data; however, these uncertainty intervals may not capture all sources of bias, including measurement bias, selection bias due to missing data, and model misspecification bias. Small improvements in the quality and availability of data have been observed since our last analysis, with the addition of high-quality estimates in countries/territories where data were previously unavailable (including Armenia, Bhutan, the Democratic Republic of the Congo, Kyrgyzstan, Rwanda, and Tanzania). Additionally, countries/territories are engaging in high-quality screening programs and serosurveys, to monitor progress (e.g., Egypt), or update older, lower-quality estimates, (e.g., Viet Nam and Nigeria). That said, paucity of data remains a problem for many parts of the world. Of 250 countries/territories in the world, only 110 countries/territories had sufficient data to generate a model. Uncertainty in treatment data is also a concern, especially in countries/territories producing generic medications (e.g., India) and countries/territories where national programmatic data are collected but only reflect the public sector. Where possible, these uncertainties have been addressed by comparing multiple sources of data (national program data, generic sales data, humanitarian program data, expert consensus). As described previously, using models to forecast 2015 and 2020 HCV prevalence runs the risk of being inaccurate. Although we report the cascade of care through calendar year 2020, the prevalence estimate is emphasized for the beginning of year 2020 to acknowledge uncertainty around country responses due to the COVID-19 pandemic. For the model forecasting, we assume two years of disrupted treatment, followed by a return to previous trends. However, some countries have reported relatively near discontinuation of new screening and diagnosis in 2020 but with only small changes to treatment in the same year. This may mean our treatment projections in future years are overly optimistic.

Conclusion —The global prevalence of HCV declined from 2015 however, there were still 57 million viremic infections remaining in 2020 with only 12.9 million diagnosed. More than 10 million people have initiated DAA therapies since 2015, with more than a third of treatments occurring in Egypt. With the Egyptian program reaching near completion in 2019, global treatment forecasts dropped substantially. Treatment further declined in 2020, partially due to the depletion of “warehoused” patients, the COVID-19 pandemic, and other factors. If treatment remains below 1 million patients per year, as is currently estimated, then liver deaths and other end-stage outcomes could be expected to increase globally by 2030. Thus, it is imperative that countries continue to pursue HCV elimination efforts through screening, diagnosis, and timely treatment. The data presented here provide a call to action for the global hepatitis community and can act as a reset point for countries revisiting HCV elimination efforts in the wake of the COVID-19 pandemic.

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Data Sharing Statement

For a period of 1 year after publication, the authors will share the data used in the maps and figures in an Excel format after written request to the corresponding author. Data sharing will be limited to government agencies, academic institutions, and non-profit organizations, and will not apply to for-profit or consulting organizations. Additionally, select country level, regional and global data from the manuscript will be available publicly on the Polaris Observatory Website <https://cdafound.org/polaris-countries-dashboard/>

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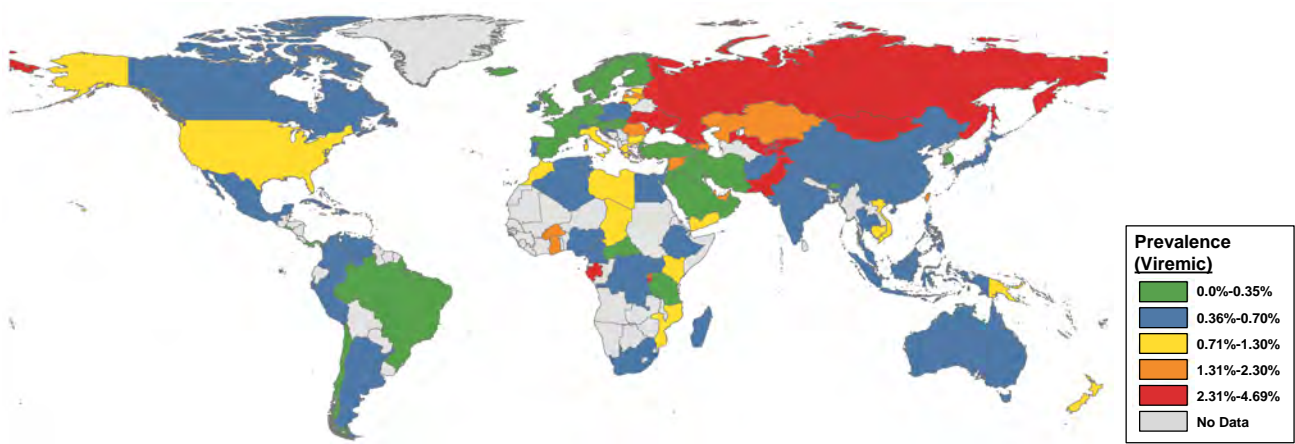
Tables (included separately)

Table 1. Modeled HCV viremic prevalence and number of viremic infections for 110 countries with approved or estimated models (all ages, 0+), beginning of years 2015 and 2020.

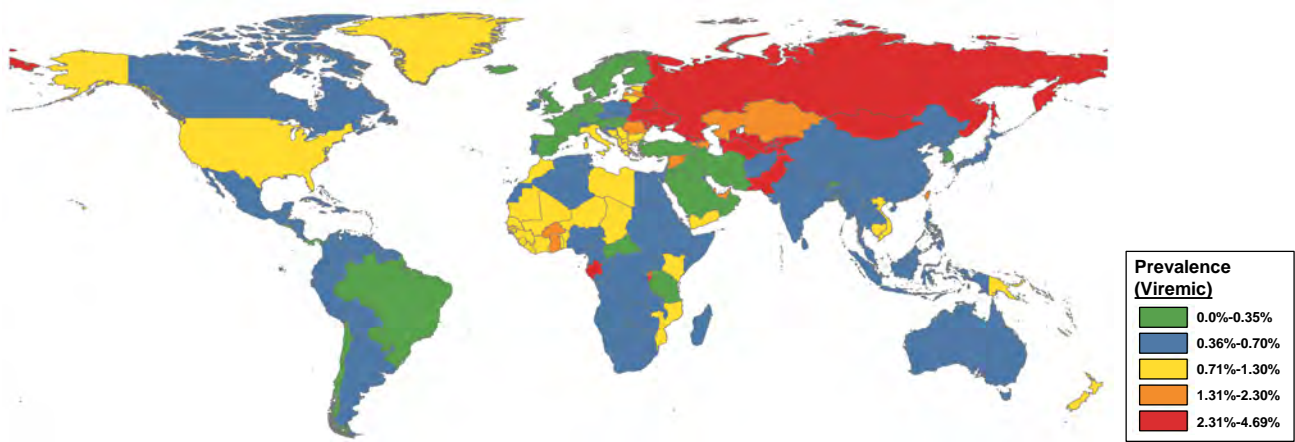
Table 2. Regional and global viremic prevalence (2015 and 2020) and annual cascade of care in 2020.

Figure 1. Evolution of country/territory HCV prevalence estimates (beginning of 2020)

A. 2020 Viremic HCV infection prevalence among countries/territories with approved or estimated models



B. Viremic HCV infection prevalence all countries/territories



C. Number of viremic HCV infections all countries/territories

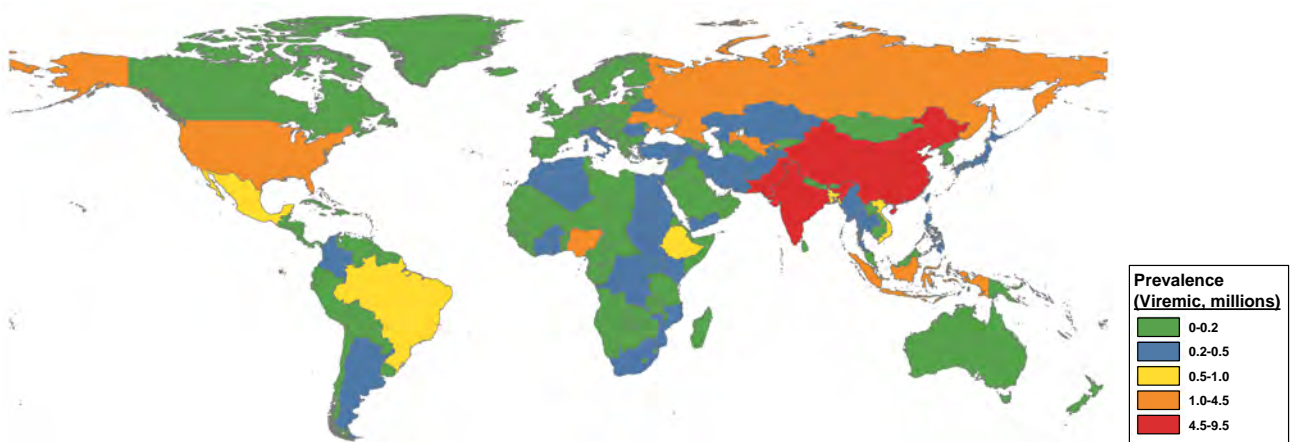
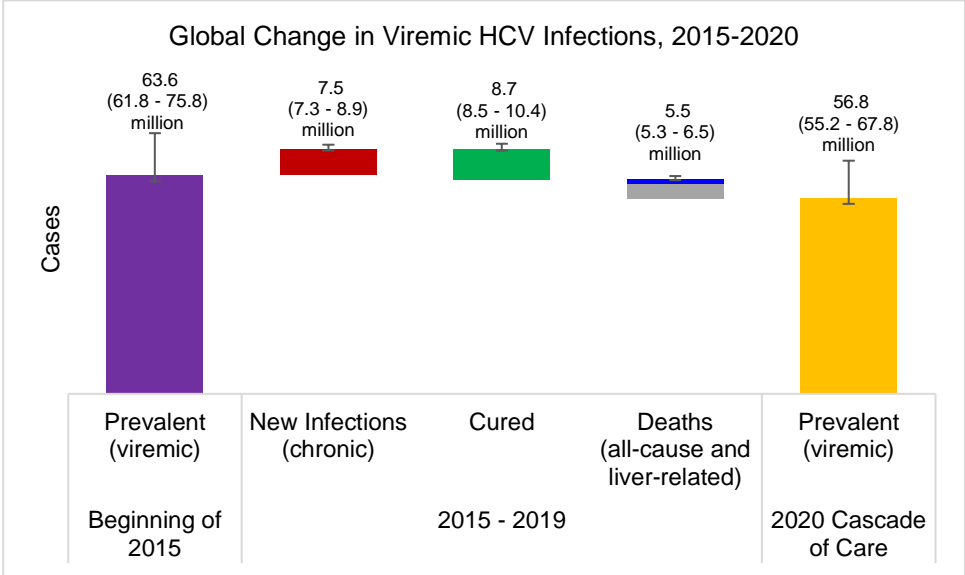


Figure 2. Change in viremic HCV infections from 2015 to 2020, a) Waterfall chart indicating the number of global viremic infections from 2015 through 2020, including the number of incident infections, treated/cured and deaths; b) Sankey diagram of viremic HCV infections in 2020, compared with viremic infections at the beginning of 2015 including the fraction attributable to treatment and cure, among countries accounting for more than 70% of viremic infections in 2015 (*bar width is proportional to the size of the population*).

a)



b)

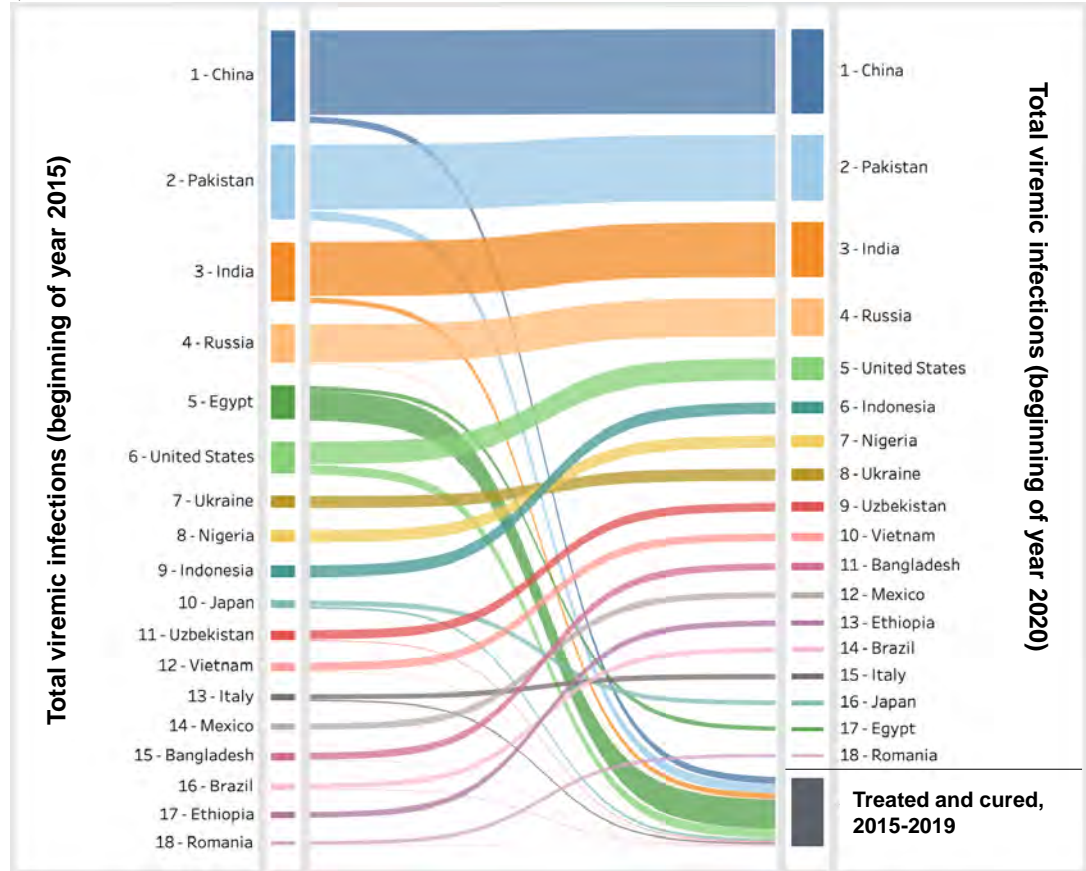


Figure 3. Cumulative and annual cascade of care from 2015 through the beginning of 2020, a) globally by income group, compared against the 2020 targets; b) globally by income group, compared against the 2030 targets; c) by individual income group, compared against the 2030 targets.

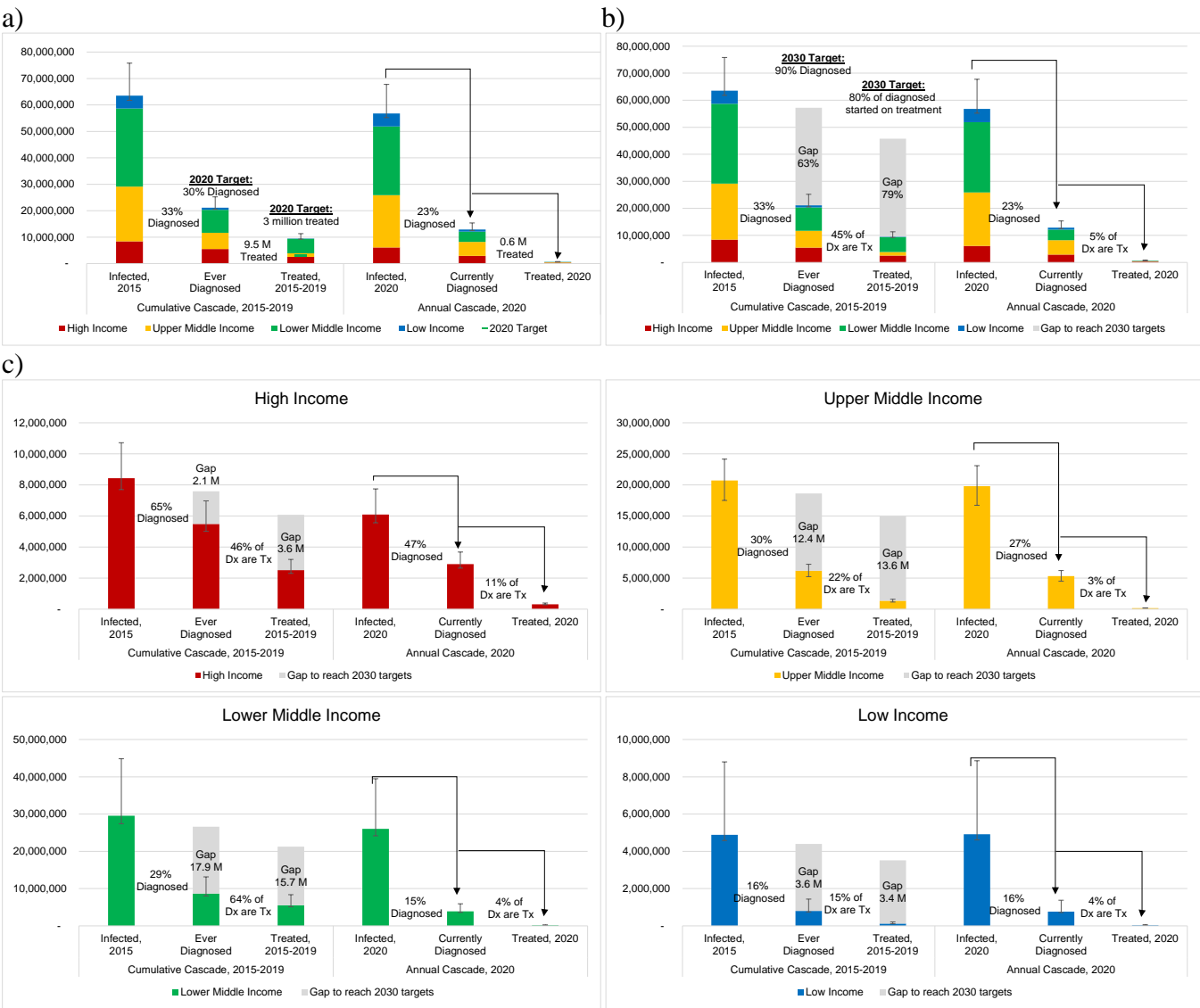


Figure 4. Cumulative number of patients initiated on treatment from 2015 through the end of 2019 for countries/territories accounting for more than 90% of treatment starts

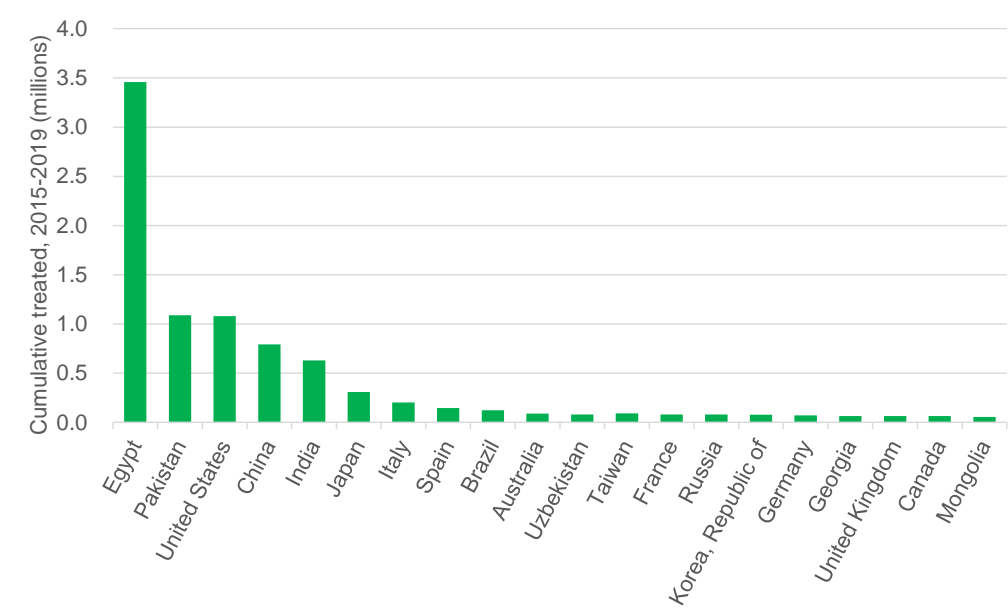
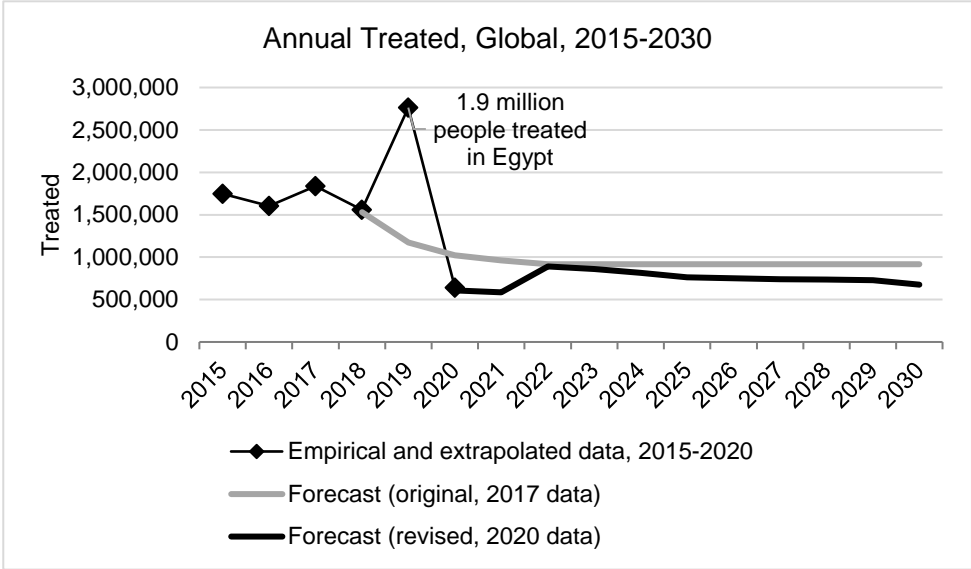
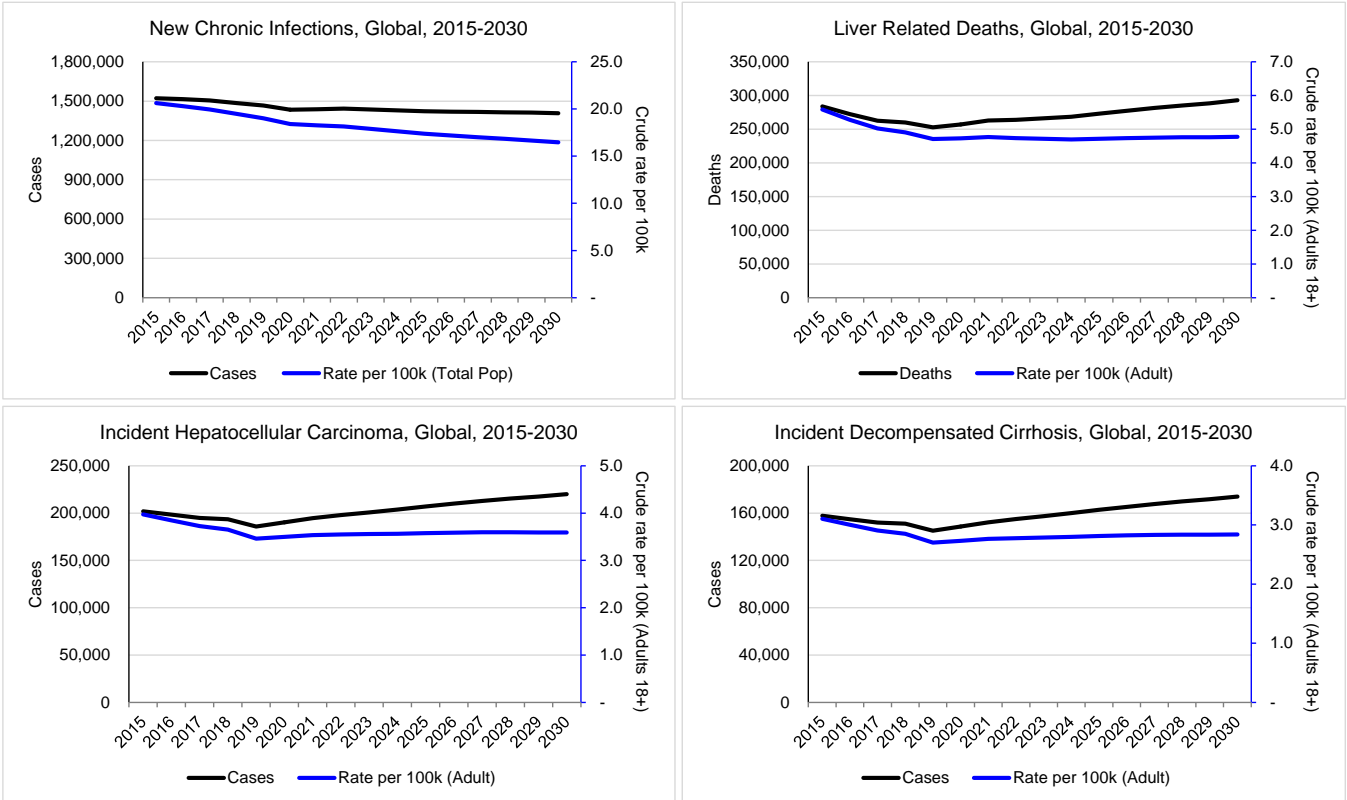


Figure 5. Global forecasts, 2015-2030 a) annual patients treated, with empirical and extrapolated data through 2020 as well global forecasts based on peak treatment in 2017 and revised forecasts based on country-level data through 2020; b) forecasted number and crude annual rate of new chronic infections, liver related deaths, hepatocellular carcinoma (HCC) and decompensated cirrhosis

a)



b)



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- 1 Evolution of country/territory HCV prevalence estimates (beginning of 2020)
- 2 Change in viremic HCV infections from 2015 to 2020
- 3 Cumulative and annual cascade of care from 2015 through the beginning of 2020
- 4 Cumulative number of patients initiated on treatment from 2015 through the end of 2019
- 5 Global forecasts, 2015-2030

Table 1. Modeled HCV viremic prevalence and number of viremic infections for 110 countries with approved or estimated models (all ages, 0+), beginning of years 2015 and 2020.

Region/Country/Territory	Viremic Prevalence in 2015 ^{i,ii} (95% UI)	Viremic Population (000) in 2015 ^{i,ii} (95% UI)	Viremic Prevalence in 2020 ^{i,ii} (95% UI)	Viremic Population (000) in 2020 ^{i,ii} (95% UI)
Asia Pacific, High Income				
Japan	0.7% (0.6%-0.9%)	1,028 (829-1,240)	0.4% (0.4%-0.5%)	562 (453-678)
Korea, Republic of	0.3% (0.2%-0.4%)	142 (115-190)	0.2% (0.1%-0.2%)	90 (73-120)
Asia, Central				
Armenia	2.4% (2.1%-3.5%)	72 (62-104)	2.2% (1.9%-3.1%)	64 (56-93)
Azerbaijan	1.9% (1.2%-2.3%)	179 (115-223)	1.9% (1.2%-2.3%)	190 (121-235)
Georgia	3.7% (3.6%-4.3%)	150 (148-177)	2.4% (2.4%-2.8%)	96 (95-113)
Kazakhstan	2.1% (1.7%-2.3%)	366 (310-415)	1.9% (1.6%-2.2%)	359 (304-407)
Kyrgyzstan	2.7% (2.3%-4.3%)	160 (137-260)	2.6% (2.2%-4.1%)	167 (142-270)
Mongolia	6.4% (5.7%-10.3%)	198 (177-317)	4.2% (3.8%-6.8%)	139 (124-223)
Tajikistan	2.8% (2.2%-3.3%)	243 (187-280)	2.7% (2.0%-3.1%)	254 (195-293)
Uzbekistan	3.1% (2.4%-3.7%)	959 (767-1,150)	3.0% (2.4%-3.6%)	1,004 (804-1,205)
Asia, East				
China, Mainland	0.7% (0.5%-0.9%)	10,023 (7,692-12,353)	0.7% (0.5%-0.8%)	9,487 (7,281-11,693)
Hong Kong	0.3% (0.1%-0.4%)	18 (5-28)	0.2% (0.1%-0.4%)	17 (4-27)
Taiwan	1.9% (1.6%-5.6%)	458 (402-1,383)	1.4% (1.2%-4.1%)	322 (283-974)
Asia, South				
India	0.5% (0.4%-1.2%)	6,427 (5,224-15,671)	0.4% (0.4%-1.1%)	6,137 (4,988-14,963)
Pakistan	3.6% (2.8%-4.9%)	7,213 (5,702-9,767)	3.3% (2.6%-4.5%)	7,395 (5,846-10,012)
Asia, Southeast				
Cambodia	1.3% (0.5%-3.3%)	207 (82-524)	1.1% (0.5%-2.9%)	190 (75-482)
Indonesia	0.5% (0.1%-1.0%)	1,302 (186-2,595)	0.5% (0.1%-1.0%)	1,364 (195-2,721)
Malaysia	0.4% (0.3%-1.6%)	135 (107-508)	0.4% (0.3%-1.5%)	127 (100-477)

Region/Country/Territory	Viremic Prevalence in 2015 ^{i,ii} (95% UI)	Viremic Population (000) in 2015 ^{i,ii} (95% UI)	Viremic Prevalence in 2020 ^{i,ii} (95% UI)	Viremic Population (000) in 2020 ^{i,ii} (95% UI)
Philippines	0.4% (0.2%-1.3%)	451 (223-1,350)	0.4% (0.2%-1.2%)	439 (217-1,314)
Thailand	0.6% (0.5%-0.8%)	381 (346-576)	0.5% (0.5%-0.8%)	378 (343-571)
Viet Nam	1.0% (0.8%-1.4%)	947 (786-1,275)	0.9% (0.8%-1.3%)	914 (759-1,231)
Australasia				
Australia	0.8% (0.7%-0.8%)	193 (174-207)	0.5% (0.4%-0.5%)	119 (108-128)
New Zealand	1.1% (0.6%-1.5%)	50 (27-72)	0.9% (0.5%-1.3%)	43 (23-62)
Caribbean				
Cuba	0.5% (0.1%-1.2%)	57 (16-142)	0.5% (0.1%-1.2%)	55 (15-138)
Dominican Republic	0.7% (0.5%-1.6%)	70 (49-168)	0.6% (0.4%-1.4%)	65 (46-157)
Puerto Rico	1.2% (0.7%-2.2%)	41 (22-72)	1.4% (0.8%-2.6%)	41 (23-74)
Europe, Central				
Bulgaria	1.3% (0.6%-2.0%)	93 (43-143)	1.2% (0.6%-1.9%)	86 (40-132)
Croatia	0.5% (0.5%-0.8%)	21 (20-33)	0.5% (0.4%-0.7%)	19 (18-29)
Czechia	0.5% (0.2%-0.6%)	53 (21-67)	0.5% (0.2%-0.6%)	55 (22-69)
Hungary	0.3% (0.3%-0.7%)	32 (24-73)	0.3% (0.2%-0.7%)	29 (22-65)
Poland	0.5% (0.3%-0.6%)	188 (129-249)	0.4% (0.3%-0.5%)	157 (108-208)
Romania	2.5% (2.4%-3.0%)	504 (479-601)	2.3% (2.2%-2.7%)	437 (415-521)
Slovakia	0.2% (0.2%-1.4%)	13 (8-78)	0.2% (0.1%-1.4%)	12 (8-74)
Slovenia	0.2% (0.1%-0.2%)	4 (3-5)	0.1% (0.1%-0.2%)	3 (2-4)
Europe, Eastern				
Estonia	1.5% (1.1%-1.8%)	20 (15-24)	1.2% (0.9%-1.4%)	16 (12-19)
Latvia	2.1% (1.5%-2.8%)	40 (28-55)	2.0% (1.4%-2.8%)	38 (27-53)
Lithuania	1.1% (0.7%-1.5%)	32 (20-45)	1.0% (0.6%-1.4%)	28 (17-39)
Russia	2.9% (1.8%-3.3%)	4,179 (2,568-4,828)	2.9% (1.8%-3.4%)	4,255 (2,614-4,915)
Ukraine	3.2% (2.6%-4.2%)	1,443 (1,172-1,893)	3.1% (2.5%-4.0%)	1,342 (1,089-1,760)

Region/Country/Territory	Viremic Prevalence in 2015 ^{i,ii} (95% UI)	Viremic Population (000) in 2015 ^{i,ii} (95% UI)	Viremic Prevalence in 2020 ^{i,ii} (95% UI)	Viremic Population (000) in 2020 ^{i,ii} (95% UI)
Europe, Western				
Austria	0.3% (0.1%-0.4%)	25 (5-39)	0.2% (0.0%-0.3%)	15 (3-23)
Belgium	0.3% (0.2%-0.6%)	31 (22-77)	0.2% (0.1%-0.5%)	24 (17-59)
Denmark	0.2% (0.2%-0.3%)	11 (10-16)	0.1% (0.1%-0.2%)	7 (6-10)
Finland	0.4% (0.3%-0.5%)	22 (17-28)	0.3% (0.3%-0.4%)	19 (15-25)
France	0.3% (0.2%-0.3%)	183 (143-234)	0.2% (0.1%-0.2%)	112 (88-143)
Germany	0.3% (0.2%-0.5%)	254 (152-457)	0.2% (0.1%-0.4%)	189 (113-340)
Greece	1.0% (0.7%-1.3%)	106 (75-136)	0.9% (0.7%-1.2%)	96 (68-123)
Iceland	0.2% (0.2%-0.3%)	0.7 (0.6-0.9)	0.1% (0.1%-0.1%)	0.3 (0.2-0.3)
Ireland	0.6% (0.4%-1.1%)	30 (20-51)	0.6% (0.4%-0.9%)	27 (18-46)
Israel	0.9% (0.6%-1.3%)	73 (47-111)	0.7% (0.5%-1.1%)	61 (39-91)
Italy	1.4% (0.6%-2.0%)	888 (388-1,298)	1.0% (0.4%-1.4%)	577 (252-843)
Luxembourg	0.9% (0.5%-1.1%)	5 (3-6)	0.8% (0.4%-0.9%)	5 (3-6)
Malta	0.3% (0.2%-0.6%)	1.2 (1.1-2.6)	0.2% (0.2%-0.4%)	0.9 (0.8-1.9)
Netherlands	0.1% (0.0%-0.2%)	20 (8-34)	0.1% (0.0%-0.1%)	14 (5-24)
Norway	0.3% (0.2%-0.5%)	14 (9-29)	0.1% (0.1%-0.3%)	7 (4-14)
Portugal	0.5% (0.5%-0.8%)	61 (55-92)	0.4% (0.4%-0.6%)	42 (38-64)
Spain	0.3% (0.2%-1.3%)	201 (112-742)	0.1% (0.1%-0.4%)	56 (31-205)
Sweden	0.4% (0.3%-0.5%)	41 (34-50)	0.3% (0.2%-0.3%)	26 (22-31)
Switzerland	0.5% (0.5%-0.5%)	44 (40-47)	0.4% (0.3%-0.4%)	32 (29-35)
United Kingdom	0.3% (0.2%-0.4%)	177 (132-247)	0.2% (0.1%-0.3%)	127 (95-177)
Latin America, Andean				
Peru	0.5% (0.3%-0.5%)	161 (104-167)	0.5% (0.3%-0.5%)	157 (101-163)
Latin America, Central				

Region/Country/Territory	Viremic Prevalence in 2015 ^{i,ii} (95% UI)	Viremic Population (000) in 2015 ^{i,ii} (95% UI)	Viremic Prevalence in 2020 ^{i,ii} (95% UI)	Viremic Population (000) in 2020 ^{i,ii} (95% UI)
Colombia	0.7% (0.6%-1.0%)	335 (314-492)	0.6% (0.6%-0.9%)	320 (300-470)
El Salvador	0.3% (0.2%-0.3%)	17 (13-20)	0.2% (0.2%-0.3%)	16 (13-19)
Mexico	0.6% (0.6%-0.7%)	790 (718-862)	0.6% (0.5%-0.6%)	751 (683-820)
Panama	0.3% (0.3%-0.4%)	13 (10-17)	0.3% (0.3%-0.4%)	14 (11-18)
Venezuela	0.6% (0.4%-0.7%)	169 (134-217)	0.6% (0.5%-0.8%)	167 (133-215)
Latin America, Southern				
Argentina	0.8% (0.3%-1.9%)	348 (131-819)	0.7% (0.3%-1.6%)	316 (119-745)
Chile	0.2% (0.0%-0.3%)	37 (6-52)	0.2% (0.0%-0.2%)	33 (5-48)
Latin America, Tropical				
Brazil	0.3% (0.2%-0.4%)	724 (391-944)	0.3% (0.2%-0.4%)	604 (326-787)
North Africa/Middle East				
Afghanistan	0.5% (0.2%-0.9%)	192 (66-317)	0.5% (0.2%-0.9%)	203 (70-335)
Algeria	0.7% (0.2%-0.9%)	288 (80-373)	0.6% (0.2%-0.8%)	278 (77-360)
Bahrain	1.2% (0.7%-1.3%)	17 (10-19)	1.0% (0.6%-1.1%)	17 (10-19)
Egypt	3.3% (2.8%-3.9%)	3,932 (3,326-4,580)	0.5% (0.4%-0.6%)	531 (449-619)
Iran	0.3% (0.2%-0.3%)	201 (135-257)	0.2% (0.2%-0.3%)	207 (139-265)
Iraq	0.4% (0.2%-2.5%)	132 (75-905)	0.3% (0.2%-2.4%)	140 (79-958)
Jordan	0.3% (0.1%-0.3%)	26 (6-32)	0.3% (0.1%-0.3%)	27 (6-33)
Lebanon	0.1% (0.0%-0.4%)	8 (3-27)	0.1% (0.0%-0.4%)	8 (3-25)
Libya	1.2% (1.1%-1.3%)	77 (70-83)	1.0% (0.9%-1.0%)	65 (60-71)
Morocco	0.9% (0.7%-1.3%)	313 (259-454)	0.8% (0.7%-1.1%)	292 (241-422)
Oman	0.4% (0.3%-0.5%)	16 (14-20)	0.3% (0.3%-0.4%)	17 (14-20)
Qatar	1.3% (1.3%-1.6%)	35 (33-41)	1.3% (1.3%-1.6%)	39 (37-45)
Saudi Arabia	0.3% (0.3%-0.8%)	106 (85-270)	0.3% (0.2%-0.7%)	97 (78-245)

Region/Country/Territory	Viremic Prevalence in 2015 ^{i,ii} (95% UI)	Viremic Population (000) in 2015 ^{i,ii} (95% UI)	Viremic Prevalence in 2020 ^{i,ii} (95% UI)	Viremic Population (000) in 2020 ^{i,ii} (95% UI)
Syria	1.5% (0.6%-3.8%)	254 (106-651)	1.6% (0.7%-4.0%)	276 (116-708)
Tunisia	0.4% (0.3%-0.6%)	46 (36-63)	0.4% (0.3%-0.5%)	44 (35-61)
Turkey	0.3% (0.2%-1.3%)	282 (162-1,029)	0.3% (0.2%-1.0%)	242 (140-885)
United Arab Emirates	1.3% (0.1%-1.8%)	118 (7-160)	1.5% (0.1%-2.1%)	152 (9-206)
Yemen	1.0% (0.6%-1.2%)	272 (165-329)	0.9% (0.5%-1.1%)	266 (161-321)
North America, High Income				
Canada	0.6% (0.4%-0.8%)	228 (144-316)	0.4% (0.3%-0.6%)	156 (99-217)
United States	0.9% (0.7%-1.3%)	3,230 (2,307-4,337)	0.8% (0.5%-1.0%)	2,494 (1,781-3,349)
Oceania				
Fiji	0.1% (0.0%-0.5%)	0.7 (0.1-4.2)	0.1% (0.0%-0.5%)	0.7 (0.1-4.2)
Papua New Guinea	1.2% (0.7%-2.0%)	101 (58-162)	1.2% (0.7%-1.9%)	104 (60-167)
Sub-Saharan Africa, Central				
Central African Republic	0.3% (0.3%-0.9%)	16 (13-41)	0.3% (0.2%-0.8%)	15 (12-39)
Democratic Republic of the Congo	0.5% (0.2%-0.9%)	413 (138-735)	0.5% (0.2%-0.8%)	418 (139-744)
Gabon	5.2% (4.7%-5.7%)	103 (95-113)	4.7% (4.3%-5.2%)	104 (96-115)
Sub-Saharan Africa, East				
Burundi	4.0% (3.6%-30.4%)	421 (377-3,190)	3.5% (3.1%-26.4%)	415 (371-3,142)
Ethiopia	0.7% (0.4%-0.8%)	683 (407-814)	0.6% (0.4%-0.7%)	684 (408-815)
Kenya	0.9% (0.3%-1.4%)	431 (133-684)	0.9% (0.3%-1.4%)	482 (149-765)
Madagascar	0.5% (0.3%-1.5%)	122 (86-376)	0.4% (0.3%-1.3%)	116 (81-357)
Mozambique	0.9% (0.4%-1.2%)	249 (124-324)	0.8% (0.4%-1.0%)	247 (123-321)
Rwanda	1.6% (0.7%-2.0%)	188 (76-226)	1.4% (0.6%-1.7%)	183 (74-221)
Tanzania	0.2% (0.2%-0.2%)	103 (83-124)	0.2% (0.1%-0.2%)	101 (81-122)
Uganda	0.6% (0.5%-0.8%)	252 (202-303)	0.6% (0.5%-0.7%)	260 (208-312)
Sub-Saharan Africa, Southern				

Region/Country/Territory	Viremic Prevalence in 2015 ^{i,ii} (95% UI)	Viremic Population (000) in 2015 ^{i,ii} (95% UI)	Viremic Prevalence in 2020 ^{i,ii} (95% UI)	Viremic Population (000) in 2020 ^{i,ii} (95% UI)
South Africa	0.5% (0.4%-1.0%)	292 (226-572)	0.4% (0.3%-0.9%)	265 (205-519)
Sub-Saharan Africa, West				
Burkina Faso	1.5% (1.4%-1.7%)	271 (267-307)	1.4% (1.3%-1.5%)	285 (281-323)
Cameroon	0.8% (0.6%-1.0%)	192 (151-242)	0.7% (0.5%-0.8%)	173 (136-218)
Chad	1.1% (0.9%-1.4%)	156 (126-204)	0.9% (0.7%-1.2%)	147 (119-193)
Gambia	0.8% (0.4%-1.6%)	18 (8-35)	0.8% (0.3%-1.5%)	18 (8-35)
Ghana	1.5% (0.8%-3.8%)	412 (236-1,082)	1.4% (0.8%-3.7%)	432 (248-1,135)
Nigeria	0.7% (0.3%-1.2%)	1,352 (496-2,234)	0.7% (0.2%-1.1%)	1,362 (500-2,251)

ⁱ 2015 and 2020 beginning of year estimates are model output projections based on historic data.

ⁱⁱ Numerators (viremic infections) and denominators (population) include all ages, 0+

Table 2. Regional and global viremic prevalence (2015 and 2020) and annual cascade of care in 2020.

Regions	2015		2020			
	Viremic Prevalence (%) (95% UI)	Viremic HCV Infected, Millions (95% UI)	Viremic Prevalence (%) (95% UI)	Viremic HCV Infected, Millions (95% UI)	Total Diagnosed, Millions (%) ⁱ	Annual Treated, 000s (%) ⁱⁱ
Global Burden of Disease (GBD Regions)						
Asia Pacific, High Income	0.7% (0.6%-0.7%)	1.2 (1.1-1.4)	0.4% (0.3%-0.4%)	0.7 (0.6-0.8)	0.5 (76%)	40.8 (6.1%)
Asia, Central	2.8% (2.6%-3.1%)	2.5 (2.3-2.7)	2.6% (2.4%-2.8%)	2.4 (2.3-2.7)	0.3 (13%)	25.8 (1.1%)
Asia, East	0.7% (0.6%-0.9%)	10.7 (9.1-12.7)	0.7% (0.6%-0.8%)	10.0 (8.6-11.9)	2.6 (26%)	114.3 (1.1%)
Asia, South	0.9% (0.8%-1.4%)	14.6 (13.3-24.3)	0.8% (0.7%-1.3%)	14.5 (13.2-24.2)	2.4 (17%)	89.6 (0.6%)
Asia, Southeast	0.6% (0.5%-0.9%)	3.9 (3.6-6.0)	0.6% (0.5%-0.9%)	3.9 (3.6-5.9)	0.5 (14%)	26.6 (0.7%)
Australasia	0.8% (0.6%-1.0%)	0.2 (0.2-0.3)	0.5% (0.4%-0.6%)	0.2 (0.1-0.2)	0.1 (87%)	9.1 (5.6%)
Caribbean	0.7% (0.4%-1.3%)	0.3 (0.2-0.6)	0.6% (0.4%-1.2%)	0.3 (0.2-0.6)	0.1 (33%)	0.7 (0.2%)
Europe, Central	0.9% (0.8%-1.2%)	1.1 (1.0-1.3)	0.8% (0.8%-1.0%)	0.9 (0.9-1.2)	0.2 (20%)	18.1 (1.9%)
Europe, Eastern	2.9% (2.3%-3.2%)	6.1 (4.9-6.6)	2.9% (2.3%-3.2%)	6.1 (4.9-6.6)	2.1 (34%)	20.5 (0.3%)
Europe, Western	0.5% (0.4%-0.6%)	2.2 (1.9-2.6)	0.3% (0.3%-0.4%)	1.4 (1.3-1.7)	0.7 (50%)	57.8 (4.0%)
Latin America, Andean	0.5% (0.2%-0.5%)	0.3 (0.1-0.3)	0.5% (0.2%-0.5%)	0.3 (0.1-0.3)	0.0 (11%)	1.8 (0.6%)
Latin America, Central	0.6% (0.6%-0.7%)	1.6 (1.4-1.7)	0.6% (0.5%-0.7%)	1.5 (1.4-1.7)	0.2 (12%)	3.7 (0.2%)
Latin America, Southern	0.6% (0.3%-1.1%)	0.4 (0.2-0.7)	0.5% (0.3%-1.0%)	0.4 (0.2-0.6)	0.0 (6%)	1.4 (0.4%)
Latin America, Tropical	0.4% (0.3%-0.4%)	0.7 (0.6-0.8)	0.3% (0.2%-0.3%)	0.6 (0.5-0.7)	0.1 (22%)	19.9 (3.2%)
North Africa/Middle East	1.2% (1.1%-1.4%)	6.6 (6.2-7.9)	0.5% (0.5%-0.6%)	3.2 (3.0-3.8)	1.1 (35%)	26.7 (0.8%)
North America, High Income	1.0% (0.8%-1.2%)	3.5 (2.8-4.2)	0.7% (0.6%-0.9%)	2.7 (2.1-3.2)	1.1 (41%)	153.1 (5.8%)
Oceania	1.1% (0.8%-3.8%)	0.1 (0.1-0.4)	1.1% (0.8%-3.6%)	0.1 (0.1-0.4)	0.0 (11%)	0.0 (0.0%)
Sub-Saharan Africa, Central	0.6% (0.4%-2.1%)	0.8 (0.4-2.5)	0.6% (0.3%-1.8%)	0.8 (0.4-2.5)	0.1 (13%)	0.0 (0.0%)
Sub-Saharan Africa, East	0.8% (0.7%-1.3%)	2.9 (2.6-4.7)	0.7% (0.6%-1.1%)	3.0 (2.7-4.8)	0.3 (10%)	26.3 (0.9%)
Sub-Saharan Africa, Southern	0.5% (0.3%-0.8%)	0.4 (0.2-0.6)	0.4% (0.3%-0.7%)	0.4 (0.2-0.5)	0.1 (22%)	0.1 (0.0%)
Sub-Saharan Africa, West	0.9% (0.7%-1.2%)	3.5 (2.6-4.7)	0.8% (0.6%-1.1%)	3.5 (2.6-4.7)	0.2 (7%)	4.3 (0.1%)

Regions	2015			2020		
	Viremic Prevalence (%) (95% UI)	Viremic HCV Infected, Millions (95% UI)	Viremic Prevalence (%) (95% UI)	Viremic HCV Infected, Millions (95% UI)	Total Diagnosed, Millions (%) ⁱ	Annual Treated, 000s (%) ⁱⁱ
World Health Organization (WHO) Regions						
African Region	0.8% (0.7%-1.2%)	7.8 (6.5-12.2)	0.7% (0.6%-1.1%)	7.8 (6.6-12.2)	0.8 (10%)	30.7 (0.4%)
Region of the Americas	0.7% (0.6%-0.8%)	6.8 (5.7-8.3)	0.6% (0.5%-0.7%)	5.7 (4.8-7.0)	1.6 (27%)	180.6 (3.1%)
Eastern Mediterranean Region	2.0% (1.7%-2.5%)	13.3 (11.4-16.5)	1.4% (1.2%-1.7%)	10.2 (8.7-12.6)	3.0 (30%)	75.1 (0.7%)
European Region	1.3% (1.1%-1.5%)	11.9 (9.8-13.5)	1.2% (1.0%-1.3%)	11.0 (9.0-12.5)	3.3 (30%)	122.4 (1.1%)
South-East Asia Region	0.5% (0.4%-1.2%)	9.7 (7.9-22.2)	0.5% (0.4%-1.1%)	9.5 (7.7-21.7)	0.8 (8%)	47.0 (0.5%)
Western Pacific Region	0.7% (0.6%-0.9%)	14.1 (12.0-17.7)	0.6% (0.6%-0.8%)	12.7 (10.8-16.0)	3.5 (28%)	184.8 (1.5%)
World Bank (WB) Income Groups						
Low Income	0.8% (0.8%-1.5%)	4.9 (4.6-8.8)	0.7% (0.7%-1.3%)	4.9 (4.6-8.9)	0.8 (16%)	28.2 (0.6%)
Lower-Middle Income	1.0% (0.9%-1.4%)	29.5 (27.4-44.8)	0.8% (0.7%-1.2%)	26.0 (24.1-39.5)	3.9 (15%)	144.5 (0.6%)
Upper-Middle Income	0.8% (0.7%-1.0%)	20.7 (17.5-24.2)	0.8% (0.6%-0.9%)	19.8 (16.7-23.1)	5.3 (27%)	159.5 (0.8%)
High Income	0.7% (0.6%-0.9%)	8.4 (7.7-10.7)	0.5% (0.5%-0.6%)	6.1 (5.6-7.7)	2.9 (47%)	308.2 (5.1%)
Total	0.9% (0.8%-1.0%)	63.6 (61.8-75.8)	0.7% (0.7%-0.9%)	56.8 (55.2-67.8)	12.9 (23%)	640.6 (1.1%)

ⁱ Proportion diagnosed was calculated as the number of total diagnosed divided by the viremic HCV infected in 2020; ⁱⁱ Proportion treated was calculated as the number of annual treated divided by the viremic HCV infected in 2020.