Modeling the Global Prevalence of Hepatitis C Virus Infection in 2015 and Genotypes

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Running title: Global prevalence of viremic HCV

Abbreviations

Genotype (G); Global Burden of Disease (GBD); Hepatitis C Virus (HCV); Hepatocellular Carcinoma (HCC); Ribonucleic Acid (RNA); Uncertainty Intervals (UI); World Health Organization (WHO)

Abstract

Background

The 69th World Health Assembly passed a resolution to eliminate hepatitis C virus (HCV) infection by 2030, which can become a reality with the recent launch of the direct acting antiviral therapies. Reliable disease burden estimates are required for national strategies. This analysis estimates the global prevalence of viremic HCV at the end of 2015, an update of the 2014 analysis, which reported 80 (64-103) million viremic infections in 2013.

Methodology

We developed country level disease burden models following a systematic review of HCV prevalence (number of studies, n = 6,754) and genotype (n = 11,342) studies published after 2013. A Delphi process was used to gain country expert consensus and validate inputs. Published estimates alone were used for countries where expert panel meetings could not be scheduled. The global prevalence was estimated by using regional averages for countries without data.

Findings

Models were built for 100 countries, 59 of which were approved by country experts, with the remaining 41 estimated using published data alone. The remaining countries had insufficient data to create a model. The global prevalence of viremic HCV is estimated to be 0·96% (95% UI: 0·84-1·07%) in 2015, corresponding to 71 (62-79) million viremic infections. Genotypes 1 and 3 were most common (44% and 25%, respectively).

Interpretation

The global estimate of viremic infections is lower than previous estimates due to more recent (lower) prevalence estimates in Africa. Additionally, increased mortality due to liver-related causes and an aging population have contributed to a reduction in infections.

This study was funded by the John C. Martin Foundation.

Keywords: Hepatitis C, global, prevalence, genotype

Research in context

Evidence before this study

In 2014, we estimated the global HCV prevalence and genotype distribution following a comprehensive review of indexed sources and grey literature (e.g., government reports) published between 2000 and 2013. The analysis focused on quantifying the number of viremic infections (HCV RNA positive). Three global prevalence studies published prior to 2014 followed a traditional systematic review and meta-analysis procedure and reported anti-HCV positive infections, which are serological evidence of past or present HCV infection.

Added value of this study

The present analysis represents both an update to and significant expansion of previous efforts to quantify the HCV prevalence and disease burden. A Delphi process was used to complement a traditional systematic review by adding a level of validation through discussions with country experts. In total, 400 experts were consulted to approve the inputs and outputs of 59 country models. This work is additionally unique in that it uses a disease burden model to forecast the 2015 year-end HCV prevalence, accounting for the impact of a changing population due to aging, treatment and cure, and mortality. In total 100 countries, representing more than 85% of the world's population, were included in the analysis. Data from these countries were used to estimate the regional prevalence, and regional prevalence rates were then applied to countries with missing data to estimate the global HCV prevalence.

Implications of all the available evidence

In 2016, the 69th World Health Assembly passed a resolution to eliminate hepatitis infection by 2030, and the World Health Organization (WHO) introduced global targets for the care and management of HCV including: "a 90% reduction in new cases of chronic hepatitis C, a 65% reduction in hepatitis C deaths, and treatment of 80% of eligible people with chronic hepatitis C infections". The global HCV prevalence rate reported in this study is much lower than previous estimates have suggested. While some of this decline can be attributed to more recent (lower) prevalence estimates in Africa, increased mortality due to liver-related causes and an aging population have also contributed to a reduction in infections. The dissemination of the data presented here is crucial for the development of national and regional strategies to achieve these international targets.

Introduction

Hepatitis C virus (HCV) infection is of growing international concern due to its substantial impact on morbidity and mortality.[1-6] A leading cause of cirrhosis, hepatocellular carcinoma (HCC), liver transplantation, and liver-related death across the globe, HCV-related disease burden continues to increase as the infected population advances to late stage liver disease.[7,8] The disease inflicts an immense health and economic burden on countries due to the infection's hepatic and extra-hepatic effects.[9-14]

In 2016, the 69th World Health Assembly passed a resolution to eliminate hepatitis infection by 2030 [15], and the World Health Organization (WHO) introduced global targets for the care and management of HCV including: "a 90% reduction in new cases of chronic hepatitis C, a 65% reduction in hepatitis C deaths, and treatment of 80% of eligible people with chronic hepatitis C infections".[16] To achieve these goals, countries need to develop national policies based on up-to-date and reliable epidemiological evidence.[17-19] However, often data are outdated and conflicting, making evidence-based policymaking and resource allocation difficult. The objective of this work was to review and analyze available data to estimate the current HCV disease burden at the national level to support countries in their efforts to develop national strategies.

In 2014, we estimated the global HCV prevalence and genotype distribution following a comprehensive review of indexed sources and grey literature (e.g., government reports) published between 2000 and 2013.[20] The analysis focused on quantifying the number of viremic infections (HCV RNA positive). In comparison, earlier studies[21-23] had reported

anti-HCV positive infections, which are serological evidence of past or present HCV infection. In 2015, the Polaris Observatory was created to monitor and forecast the disease burden for hepatitis B and C.[24] This analysis builds upon the previous efforts with an updated literature review and the addition of disease burden modeling to develop more accurate estimates of 2015 year-end viremic HCV prevalence at the country level and aggregated to the global level.

Methods

The present analysis represents the integration of a literature review, a Delphi process that used country expert interviews to identify missing inputs and to approve all inputs/outputs, and modeling to estimate 2015 HCV prevalence. The details of the data collection, scoring of data sources, Delphi process and modeling, beyond the description in this section, are summarized in the Supplement.

Systematic Literature Review and Data Quality Scoring

Available published data between January 1, 2000 and March 31, 2016 were identified through searches of PubMed, EMBASE, and non-indexed reports (Supplement, Sections 3). Non-indexed government reports, personal communication with country 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. Articles were scored based on how well they could be extrapolated to the general population, the study sample size, and the year of analysis.[20]

HCV Disease Burden Modeling and Delphi Process

From a methodological perspective, the biggest difference between the present and previous analysis is the use of a Markov model to estimate the HCV prevalence in 2015. The reason for this addition is that HCV prevalence changes over time.[25-27] After culling and scoring available studies, a Microsoft Excel® (version 2007)- based Markov-type model, described previously[25-27], was populated with the highest-scoring epidemiological data for the country of interest (Supplement, Section 4).

Approved: A Delphi process was used to gain country expert consensus and validate inputs (Supplement, Section 5). Experts were identified through HCV-related scientific contributions, or through referrals and recommendations from leading researchers. Two or more meetings were held to get consensus around input variables and outputs, and validate the outputs against available empirical data.

Estimated: For countries where meeting with local experts could not be scheduled, published estimates were used. All published studies were reviewed and scored by two epidemiologists, and the highest scored study was used for modeling (Supplement, Section 7). When input other than prevalence rate was unavailable for a country, input was extrapolated from countries within the same Global Burden of Disease (GBD) region.

Global and Regional HCV Viremic Prevalence and Genotype Distribution

GBD regional prevalence and genotype were calculated as the weighted average of the 2015 outputs from approved and estimated models, and the regional rates were then applied to the 2015 populations of countries with missing data to estimate the global HCV prevalence and genotypes. Countries without a formal GBD designation were assigned an imputed GBD region (Supplement, Section 6).

Sensitivity Analysis

Uncertainty intervals and sensitivity analyses were conducted using Crystal Ball® (Release 11.1.3708.0), an Excel® add-in by Oracle®. Beta-PERT distributions [28] were used for all uncertain inputs. Monte Carlo simulation was used to estimate 95% uncertainty intervals (UI). It was assumed that prevalence uncertainty estimates in all countries were independent. The uncertainty range for each country was calculated based on range inputs for prevalence, transition rates, and mortality rate (Supplement, Sections 2 & 7). These were used to calculate regional and global uncertainty ranges. For these estimates, two sources of uncertainty had to be taken into consideration – country level uncertainty in prevalence and their impact on the regional/global prevalence. The 2015 country prevalence estimates and 95% UIs were consolidated and defined as assumption variables. A 1/0 switch was developed to include or exclude countries from the regional prevalence calculation, and was also defined as an assumption. A sensitivity analysis was run to identify countries that accounted for the greatest variation in the base global prevalence through their estimated prevalence uncertainty and their inclusion in regional averages.

This study was funded by the John C. Martin Foundation through the Polaris Observatory. The funders had no role in the study design, data collection, and analysis, interpretation of data, decision to publish, or preparation of the manuscript. CE, DRS, HN, HR, IG, JG, JDS, KP, KRS, KM, SB, and SR had access to the raw data. The corresponding author had full access to all of the data and the final responsibility to submit for publication

Results

Systematic Review – 9,177 studies were identified through PubMed (n = 4,556) and EMBASE (n = 4,621) with a publication date between January 1, 2013 and March 31, 2016. Following the removal of duplicates (n = 2,408), 6,754 studies were selected for review and inclusion in the final analysis. When combined with prevalence studies published prior to 2013 [20] and expert input, prevalence estimates were available for 113 countries, accounting for 92% of the world's population. Among all countries with a prevalence estimate, viremic rate was available for 81 countries, and age and gender distributions were available for 89 countries, accounting for 82% and 85% percent of the world's 2015 population, respectively (Supplement, Section 7).

The literature search for genotype data identified 11,342 studies through PubMed and EMBASE, and the results were combined with unpublished data provided by country experts. Genotype distribution was available for 115 countries (Table 1 and Supplement, Section 8), which accounted for 90% of the world's 2015 population.

Modeled Countries – Models were built for 100 countries – the inputs and outputs for 59 were *approved* by country experts and 41 were *estimated* using published data alone. To develop a model, at least one high quality prevalence study and one or more supporting inputs (i.e., age and gender, genotype, viremic rate, treatment rate) were necessary. The remaining countries had insufficient data to create a model.

The evolution of the analysis is shown in Figure 1. Figure 1A shows countries with *approved* and *estimated* modeled-prevalence as well as countries whose prevalence was extrapolated from regional averages. For *approved* and *estimated* countries, the quality score of input prevalence data is shown in Figure 1B. The 2015 viremic HCV prevalence of the same countries is shown in Figure 1C, while the prevalence of all countries, including those with an extrapolated prevalence, is shown in Figure 1D. The number of HCV infections by country is shown in Figure 1E.

The numerical prevalence and total infections for *approved* and *estimated* countries 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 in Supplement, Section 7.

Global Forecasts – The global prevalence of viremic HCV is estimated to be 0·96% (95% UI: 0·84-1·07%) in 2015, corresponding to 71 (62-79) million viremic infections. Regional estimates for HCV prevalence in 2015 are shown in Table 2. The countries which accounted for 80% of total global HCV infections are shown in Figure 2.

Sensitivity Analysis – The top ten country level uncertainties that made the largest contribution to the global uncertainty are shown in Figure 3. The top ten uncertainties listed account for 92% of the total variance in the global prevalence.

A separate sensitivity analysis looked at the impact of excluding *estimated* countries from the analysis and basing the global prevalence on *approved* countries only. In this scenario, the estimated global prevalence would be 0·7% (0·6-0·8%) with a total number of HCV infections of 38 (34-41) million.

Genotype Distribution – The HCV genotype distribution of the modeled countries is shown in Table 1. These distributions were based on published studies referenced in the Supplement, Section 8. The latter table contains data on data quality scores of the underlying study and sources for G1a/G1b breakout if they were not reported in the primary study. The estimated genotype distribution by GBD region is shown in Figure 4, while the data are combined with total viremic HCV infections by GBD region and shown in Figure 1F.

Discussion

The present analysis represents both an update to and significant expansion of previous efforts to quantify the HCV prevalence and disease burden. A Delphi process was used to complement a traditional systematic review by adding a level of validation through discussions with country experts. In total, 400 experts were consulted to approve the

inputs and outputs of 59 country models. This work is additionally unique in that it uses a disease burden model to forecast the 2015 year-end HCV prevalence, accounting for the impact of a changing population due to aging, treatment and cure, and mortality.

The 2015 global prevalence estimate of 0·96% (0·84-1·07%) or 71 (62-79) million infections is substantially lower than previous estimates.[22,23] Previous studies were based on older and higher prevalence estimates for China and India (Figure 5). However, the more recent studies[17,29] show a much lower infection rate in each country. In addition, most studies are conducted in the adult population; however, when estimates are applied to a country's total population, disease burden is overestimated. Finally, the earlier studies reported anti-HCV prevalence that is evidence of past or present infection (rather than active infections). Our previous estimate took all these factors into account for a global estimate of 80 (64-103) million viremic infections.[20] Since the last study, we completed interviews in 59 countries, and Nigeria and Cameroon reported much lower HCV prevalence based on unpublished national studies. This reduced the overall prevalence in the region. In addition, the modeling took into consideration the impact of mortality (liver-related and all cause) and treatment. The overall impact was a reduction in the global prevalence estimate, which was still within the uncertainty intervals of our previous estimate.[20] The current estimate does report a more narrow uncertainty range as a result of the updated methodology and incorporating country interviews.

Modeling the prevalence captured the change in the epidemiology of the HCV infection. As shown in Figure 6, globally, the total number of viremic HCV infections has been

decreasing since 2007; however, there were significant variations between regions. Of the modeled countries, ten showed a ≥10% growth in prevalence since 2007 due to foreign workforce from endemic countries (Qatar, and UAE), iatrogenic infections (Azerbaijan, India, Iraq, Syria, and Uzbekistan), and infections among people who inject drugs (Iran, Russia, and Latvia). In most other countries, mortality (all cause and liver related) was higher than new infections leading to a decrease in total infections over the same period. Historically, prevalence was increasing in every region until blood screening started in early to mid 1990's.

However, developing an accurate global estimate remains a problem due to lack and quality of data. Of 250 recognized countries in the world, HCV prevalence estimates were available for 113 countries (not all countries were modeled due to lack of available secondary data needed for a model). Globally, 91 countries have a population less than 1·5 million and only eight of these countries reported their HCV prevalence. Sixty percent (n=92) of the countries with a larger population had HCV prevalence studies. Of these, 21 countries had studies with a quality score of 3, 49 had a quality score of 2, and 22 had a quality score of 1 (Figure 1B, Supplement, Section 7). Thirteen of the countries with a quality score of 1 were in Europe and included Austria, Germany, Italy, Belgium, Portugal, Finland, and Norway and twenty were high income countries. Thus, the quality of the epidemiology data did not correlate with counties' income and robust national surveillance study in the general population are needed to better quantify HCV burden. Larger countries had much larger impact on the global estimates. China (quality score =

3), Pakistan (score = 3), India (score = 1), Egypt (score = 3), Russia (score = 2), and USA (score = 3) accounted for 51% of total HCV infections globally (Figure 2).

The sensitivity analysis (Figure 3) illustrates the impact of uncertainties on the global prevalence. Of all the uncertainties considered, the uncertainty in the total number of infections in India had the largest impact on our forecast. If the total number of infections in India is 11·0 million, rather than 6·2 million, the global estimate would be 76·6 million infections instead of 71·1 million. This takes into account the additional infections in India as well as the impact of India's prevalence on the regional prevalence, which is then applied to countries without data. Removing India's prevalence completely and using the regional prevalence instead (for India and other countries in the region without data) was the third largest driver of uncertainty. The global prevalence would be 75·9 million in this case, since other countries in the region (with data) have a higher prevalence than India, and regional prevalence is dampened by India. A similar observation is made in Sub-Saharan Africa-Central region, where only the Central African Republic (prevalence 0·3%) and Gabon (7·04%) had reported prevalence estimates. Removing the former from the analysis would result in Gabon being used for the regional average and an estimate of 76·7 million infections globally (Figure 3).

The prevalence range reported above does capture all uncertainties considered. Future revisions will most likely come from estimates for countries without reported studies (grey countries in Figure 1C), which included a large number of countries in Africa as well as some in Central and South America and Eastern Europe. As illustrated above,

country interviews can provide more recent unpublished prevalence estimates. To test the impact of having *approved* estimates, a sensitivity analysis was conducted where all *estimated* (non-approved) countries were removed from the analysis. In this scenario, the total estimated number of infections (globally) was 38 million. This result may be explained by a selection bias as a result of interviews being conducted in countries with a low prevalence.

Overall, care was taken to minimize biases that could have the largest impact on the global estimate. In 59 countries, interviews with country experts were used to identify relevant unpublished data and approve inputs/outputs. Panel meetings run the risk of confirmation, observer, and recall bias; however, facilitator training and meeting structure were designed to minimize the impact of these biases. Over the course of the project, ten facilitators were trained to lead country interviews. Each meeting required two attendees, one facilitator, and one note-taker. After each meeting, the note-taker provided feedback on how to improve future facilitations. In addition, for all models, the data inputs, model calibration, and outputs were reviewed by a second independent epidemiologist before being incorporated into the global estimate.

The genotype distribution, by region, did not change significantly (Figure 4) since the last study[20] with the exception of further refinement of genotype 1 (G1). When G1a and G1b were not available in the highest scored study, secondary studies were used. This refinement was requested by experts since these sub-genotypes still show a different response rate to the available therapies. A new analysis was also added (Figure 1F) that

combined genotypes and total infections by region. At a global level, G1 dominated (44% of all infections), followed by G3 (25%) and G4 (15%). G1 dominated in high and high middle income countries (60% of all infections), while G3 (36%) was common in low middle income countries, and G4 (45%) was common in low income countries. This highlights the importance of pan-genotypic therapies for elimination of HCV.

Many of the limitations of the original study[20] were addressed here; however, there remained a number of limitations. As mentioned above, availability of data and the quality of available data limited the accuracy of the forecasts (especially in Sub-Sahara Africa). Ranges were used to address the uncertainty in the available data. In addition, in the modeled countries the treated population was segmented by genotype proportionally to the genotype distribution of the HCV infected population. If individuals with specific genotypes were treated preferentially, then the genotype distribution of the prevalent population could be different than what is forecasted here. The use of a model to forecast 2015 HCV prevalence introduced another limitation – the accuracy of the model. When available, the outputs of the model were validated against empirical data to reduce errors due to the modeling. However, another limitation was the uncertainty in empirical data. Two recent studies have shown that HCC cases are under-reported by 37-50% in Sweden and Melbourne, Australia.[30,31] This would result in an underestimation of HCC cases by our models.

There has been much discussion regarding the lower HCV prevalence estimates of our studies as compared to previous studies.[22,23] It is important to point out that over half of

the countries included in this analysis were reviewed and approved by experts in each country. We forecast a continual decline in total HCV infections as we move forward. In 2015, an estimated 950,000 patients were treated for HCV, with two thirds of those treatments with direct acting anti-viral.[24] An estimated 700,000 individuals achieved sustained viral response and were removed from the infected population. This accounts for only 1% of the total infected population who are treated and cured annually. However, as countries develop their national hepatitis elimination strategies and expand prevention, screening, and treatment, a more rapid decline in total viremic infections is forecasted.

Declaration of Interests

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Tables

Table 1. Modeled 2015 HCV viremic prevalence/chronically infected population (all ages) and genotype distribution

Region/ Country	Viremic Prevalence in 2015[i]	Viremic Population (000) in 2015[i]	Genotypes[ii]									
			1a	1b	1c	1 (Other)	2	3	4	5	6	Mixed/ Other
Asia Pacific, High Income												
Japan	0·7% (0·3%-0·8%)	857 (364-1,024)		64·8%			34·2%					1·0%
Korea, Republic of	0·5% (0·3%-0·5%)	231 (148-261)	3·0%	45·4%		4·3%	45·3%	0·8%	0·2%		1·0%	
Asia, Central												
Armenia			5·2%	36·2%		1·7%	18·9%	38·0%				
Azerbaijan	1·9% (1·3%-2·1%)	190 (125-212)	2·9%	64·2%			6·7%	26·0%	0·2%			
Georgia	4·2% (3·0%-4·2%)	165 (120-169)	1·9%	37·6%			24·5%	34·3%				1·7%
Kazakhstan	2·8% (1·9%-3·2%)	508 (334-572)	2·5%	52·5%			10·0%	35·0%				
Mongolia	6·4% (4·3%-7·9%)	194 (131-237)		98·8%			1·2%					
Tajikistan				82·7%			5·8%	7·7%				3·8%
Uzbekistan	4·3% (3·0%-5·0%)	1,292 (902-1,524)	2·9%	64·2%			6·7%	26·0%	0·2%			
Asia, East												
China	0·7% (0·5%-0·8%)	9,795 (6,675-10,832)	1·4%	56·8%			15·4%	8·7%			6·3%	11·4%
Hong Kong	0·2% (0·1%-0·3%)	15 (6-22)	4·3%	62·4%			3·2%	2·8%			27·4%	
Taiwan	2·1% (1·3%-3·7%)	489 (310-877)	2·6%	45·5%		0·7%	39·5%	1·0%	0·2%		0·5%	10·1%
Asia, South												
Afghanistan	0·5% (0·3%-0·8%)	181 (85-258)	35·2%	2·8%				62·0%				
India	0·5% (0·4%-0·8%)	6,245 (4,748-10,957)	9·0%	16·1%		3·3%		64·1%	7·3%	0·3%		
Nepal			11·3%	6·6%		21·4%		58·4%				2·4%
Pakistan	3·8% (2·8%-3·9%)	7,172 (5,363-7,487)	4·8%	1·2%		1·0%	3·8%	79·0%	1·6%	0·1%	0·1%	8·3%
Asia, Southeast												
Cambodia	1·6% (0·9%-1·7%)	257 (147-272)		24·0%				20·0%			56·0%	
Indonesia	0·5% (0·2%-0·8%)	1,289 (443-2,046)	25·6%	39·0%		3·0%	9·3%	9·4%	3·6%			10·0%
Laos				4·4%							95·6%	
Malaysia	1·2% (0·8%-1·3%)	382 (240-405)				35·8%	0·7%	62·3%	0·7%		0·4%	
Myanmar			4·1%	6·9%			0·7%	39·3%			49·0%	

Region/ Country	Viremic Prevalence in 2015[i]	Viremic Population (000) in 2015[i]	Genotypes[ii]									
			1a	1b	1c	1 (Other)	2	3	4	5	6	Mixed/ Other
Philippines	0·6% (0·3%-0·6%)	614 (353-651)	70·7%	2·5%			26·4%		0·2%		0·2%	
Sri Lanka				46·9%			37·5%					15·6%
Thailand	0·7% (0·4%-0·7%)	463 (255-487)	4·4%	13·0%				47·8%			34·8%	
Vietnam	1·1% (0·6%-1·2%)	1,066 (580-1,116)	30·0%	17·1%			1·1%	1·1%			50·8%	
Australasia												
Australia	1·0% (0·7%-1·0%)	230 (178-244)	18·5%	15·7%		15·4%	5·6%	42·2%	1·3%		1·1%	0·2%
New Zealand	1·0% (0·6%-1·3%)	48 (30-62)	44·0%	11·0%			7·0%	35·0%			1·0%	2·0%
Caribbean												
Cuba	0·3% (0·1%-0·7%)	35 (14-77)	17·0%	81·0%								2·0%
Dominican Republic	0·6% (0·4%-1·0%)	68 (42-108)	58·9%	19·4%		3·7%	9·6%	0·5%	0·2%			7·7%
Guadeloupe	0·3% (0·2%-0·6%)	1 (1-3)				80·0%		20·0%				
Martinique			23·6%	56·7%	0·9%		6·9%	7·8%	3·6%	0·3%	0·3%	
Suriname							100·0%					
Europe, Central												
Albania			6·0%	50·0%			20·0%	8·0%	16·0%			
Bosnia and Herzegovina			4·0%	69·3%			4·0%	21·3%	1·3%			
Bulgaria	1·2% (0·7%-1·6%)	87 (46-122)	5·3%	72·3%				11·6%				10·8%
Croatia	0·6% (0·4%-0·7%)	26 (17-28)	13·1%	37·4%		8·3%	2·2%	35·6%	3·4%			
Czech Republic	0·4% (0·2%-0·5%)	43 (22-49)	13·2%	52·8%			0·5%	31·1%	2·4%			
Hungary	0·5% (0·3%-0·6%)	52 (29-55)	9·1%	79·9%		1·6%	0·9%	6·7%	1·7%	0·1%		
Macedonia						55·4%		44·6%				
Montenegro			19·6%	35·0%			1·1%	24·7%	19·6%			
Poland	0·5% (0·4%-0·6%)	184 (136-224)	2·0%	83·0%			0·1%	10·0%	4·9%			
Romania	2·5% (1·8%-2·6%)	547 (397-566)	5·4%	92·6%				0·8%	1·2%			
Serbia						57·9%%	3·7%	23·2%	6·7%			8·5%
Slovakia	0·6% (0·4%-0·7%)	33 (20-37)				89·9%	1·5%	6·6%	0·5%		0·5%	1·0%
Slovenia	0·3% (0·2%-0·3%)	6 (4-7)	6·9%	8·2%		53·0%	2·1%	29·3%	0·4%	0·1%		
Europe, Eastern												
Belarus			5·0%	53·2%			2·5%	25·7%	13·6%			

Region/ Country	Viremic Prevalence in 2015[i]	Viremic Population (000) in 2015[i]	Genotypes[ii]									
			1a	1b	1c	1 (Other)	2	3	4	5	6	Mixed/ Other
Estonia	1·4% (0·9%-1·6%)	18 (12-20)	1·0%	71·7%			3·0%	24·2%				
Latvia	2·2% (1·4%-2·6%)	43 (28-50)	46·1%	4.3%		13·4%	3·6%	31·9%	0·7%			
Lithuania	1·1% (0·7%-1·3%)	33 (20-39)	2·1%	69·3%		3·8%	5·6%	19·2%				
Russia	3·3% (2·3%-3·5%)	4,748 (3,238-4,960)	2·1%	52·8%			8·1%	36·3%	0·1%			0·6%
Ukraine			1·6%	42·1%			1·6%	28·8%	0·8%			25·1%
Europe, Western												
Austria	0·2% (0·1%-0·4%)	21 (6-30)	20·0%	52·0%			5·0%	19·0%	4·0%			
Belgium	0·6% (0·2%-0·7%)	64 (23-75)		50·0%		9·0%	6·0%	19·0%	14·0%	2·0%		
Denmark	0·3% (0·3%-0·3%)	19 (14-20)	34·0%	12·0%			8·0%	43·0%	3·0%			
Finland	0·4% (0·3%-0·5%)	23 (16-26)	10·2%	11·6%		3·3%	11·4%	48·8%	0·9%	0·1%	0·1%	13·6%
France	0·3% (0·1%-0·3%)	194 (93-222)	14·8%	29·7%		15·3%	9·1%	19·7%	9·2%	2·0%	0·2%	
Germany	0·3% (0·1%-0·4%)	205 (90-313)	25·0%	33·0%		4·0%	6·4%	27·4%	3·3%	0·2%	0·2%	
Greece	1·1% (0·7%-1·5%)	132 (82-169)	11·5%	28·4%	0·2%	5·1%	7·0%	34·0%	13·9%			
Iceland	0·3% (0·2%-0·4%)	1 (1-1)	41·1%	1·8%			0·8%	55·3%	1·0%			
Ireland	0·6% (0·4%-0·9%)	30 (20-42)	42·0%	14·0%			4·0%	39·0%	1·0%			
Israel	1·2% (0·7%-1·3%)	100 (60-103)	12·0%	57·0%			8·0%	20·0%	3·0%			
Italy	1·1% (0·7%-2·7%)	680 (455-1,641)	11·0%	44·0%		3·0%	15·0%	10·0%	7·0%			10·0%
Luxembourg	0·9% (0·6%-1·0%)	5 (3-6)				55·3%	4·3%	33·6%	6·4%			
Malta	0·3% (0·2%-0·4%)	1 (1-2)	45·0%	15·0%			1·0%	37·0%	2·0%			
Netherlands	0·1% (0·0%-0·2%)	16 (5-26)	14·8%	15·6%		18·8%	9·7%	29·3%	10·5%			1·3%
Norway	0·4% (0·3%-0·5%)	21 (15-24)	18·0%	18·0%		4·0%	9·0%	50·0%	1·0%			
Portugal	0·8% (0·7%-1·1%)	89 (74-120)	42·7%	21·4%		4·0%	1·3%	17·9%	12·5%			0·2%
Spain	0·8% (0·3%-1·2%)	386 (159-557)	24·0%	53·5%			2·0%	8·2%	9·7%			2·5%
Sweden	0·4% (0·3%-0·4%)	38 (28-43)	40·0%	10·0%			20·0%	30·0%				
Switzerland	1·0% (0·6%-1·1%)	78 (45-87)	26·0%	26·0%			8·5%	29·2%	10·3%			
United Kingdom	0·3% (0·1%-0·3%)	189 (91-211)	24·4%	11·9%		8·8%	7·3%	43·8%	3·8%			

Region/ Country	Viremic Prevalence in 2015[i]	Viremic Population (000) in 2015[i]	Genotypes[ii]									
			1a	1b	1c	1 (Other)	2	3	4	5	6	Mixed/ Other
Latin America, Andean												
Peru	0·5% (0·3%-0·6%)	167 (99-182)	74·0%	12·0%			2·0%	10·0%				2·0%
Latin America, Central												
Colombia	0·8% (0·6%-0·9%)	409 (272-436)	5·7%	82·8%			8·5%	2·8%				
Mexico	0·4% (0·3%-0·5%)	532 (304-557)	45·4%	24·9%			21·8%	7·2%	0·3%	0·1%		0·0%
Panama	0·3% (0·2%-0·3%)	12 (7-14)										
Venezuela	0·4% (0·2%-0·4%)	118 (59-126)	37·0%	26·0%		0·4%	33·0%	4·0%				
Latin America, Southern												
Argentina	0·8% (0·3%-1·2%)	326 (144-490)	20·3%	38·1%		0·8%	21·7%	17·8%	1·3%			
Chile	0·3% (0·2%-0·5%)	57 (31-94)	7·9%	72·7%			2·0%	16·5%	0·6%	0·3%	0·1%	
Latin America, Tropical												
Brazil	0·9% (0·6%-0·9%)	1,787 (1,293-1,896)	31·0%	33·4%		0·4%	4·6%	30·2%	0·2%	0·1%		
North Africa/Middle East												
Algeria	1·0% (0·3%-1·7%)	388 (140-674)	1·4%	86·2%		1·2%	8·5%	0·9%	1·2%	0·2%		0·5%
Bahrain	1·2% (0·8%-1·3%)	17 (11-18)	14·1%	21·1%		1·6%	3·9%	15·6%	25·0%			18·8%
Egypt	6·3% (4·5%-6·7%)	5,625 (4,007-6,044)		4·0%		6·0%			90·0%			
Iran	0·2% (0·2%-0·3%)	199 (129-226)	39·7%	12·1%		1·3%	1·4%	27·7%	0·9%			16·9%
Iraq	0·2% (0·2%-0·3%)	85 (60-97)	1·4%	12·9%				17·1%	52·9%			15·7%
Jordan	0·3% (0·1%-0·4%)	25 (11-29)	23·1%	19·2%					57·7%			
Kuwait						15·0%	2·5%	2·5%	80·0%			
Lebanon	0·2% (0·1%-0·4%)	8 (3-18)	6·6%	40·4%			3·7%	14·1%	33·8%	1·4%	0·1%	
Libya	0·7% (0·5%-0·7%)	42 (32-43)	4·2%	6·4%		6·9%	7·0%	7·4%	14·6%	0·0%		53·5%
Morocco	0·8% (0·5%-0·9%)	263 (190-328)	6·5%	40·3%			41·6%	1·0%	0·6%	0·1%		10·0%
Oman	0·4% (0·3%-0·4%)	16 (12-18)	5·5%	30·0%		10·1%	2·1%	32·6%	16·5%			3·2%
Palestine			18·5%	9·8%					64·1%			7·6%
Qatar	1·6% (1·3%-1·8%)	38 (30-40)	1·9%	10·7%		3·6%	0·9%	10·3%	72·4%	0·1%		
Saudi Arabia	0·3% (0·2%-0·9%)	105 (79-189)				38·6%	3·6%	5·2%	52·6%			
Syria	3·0%	554	3·4%	18·8%		6·3%	0·8%	1·8%	59·0%	10·0%		

Region/ Country	Viremic Prevalence in 2015[i]	Viremic Population (000) in 2015[i]	Genotypes[ii]									
			1a	1b	1c	1 (Other)	2	3	4	5	6	Mixed/ Other
	(1·3%-3·5%)	(245-653)										
Tunisia	0·9% (0·2%-1·1%)	108 (25-123)	5·1%	76·6%			5·1%	3·7%	7·3%			2·2%
Turkey	0·6% (0·3%-1·0%)	492 (271-763)	12·9%	80·4%			1·5%	3·7%	1·5%			
United Arab Emirates	1·3% (0·5%-1·6%)	131 (50-159)	5·4%	9·4%		25·6%	2·2%	35·0%	22·0%			
Yemen	0·8% (0·5%-0·9%)	211 (143-258)										
North America, High Income												
Canada	0·6% (0·4%-0·7%)	212 (136-246)	36·5%	21·5%		6·1%	14·1%	20·2%	0·3%			1·3%
Puerto Rico	1·0% (0·6%-1·6%)	36 (23-60)	39·8%	27·1%		15·2%	12·1%	3·8%	1·8%		0·2%	
United States	0·9% (0·7%-1·2%)	2,936 (2,231-3,826)	46·2%	26·3%			10·7%	8·9%	6·3%		1·1%	0·5%
Oceania												
Papua New Guinea	1·2% (0·9%-4·2%)	94 (70-328)										
Samoa	0·1% (0·1%-0·2%)	0·2 (0·1-0·4)										
Sub-Saharan Africa, Central												
Central African Republic	0·3% (0·2%-0·4%)	16 (11-18)					8·6%	8·6%	82·8%			
Congo, Democratic Republic of the							3·2%		96·8%			
Equatorial Guinea						35·0%	1·7%	3·3%	60·0%			
Gabon	7·0% (5·1%-7·3%)	124 (90-129)				5·8%	2·2%		92·0%			
Sub-Saharan Africa, East												
Burundi	1·0% (0·8%-4·0%)	120 (93-459)	5·6%					1·7%	92·7%			
Ethiopia	0·6% (0·4%-0·7%)	647 (410-726)	8·8%	2·7%		2·0%	13·5%	9·5%	60·0%			3·5%
Kenya	0·2% (0·1%-0·3%)	115 (42-126)	10·0%				90·0%					
Madagascar	0·2% (0·2%-0·3%)	56 (39-81)		52·9%			47·1%					
Mozambique			27·8%	22·2%				22·2%		27·8%		
Sub-Saharan Africa, Southern												
South Africa	0·7% (0·4%-0·9%)	356 (227-441)	2·3%	22·1%		7·1%	1·2%	12·6%	12·4%	35·7%		6·7%
Sub-Saharan Africa, West												
Burkina Faso	1·3% (1·0%-1·4%)	247 (189-256)	3·1%	9·4%			56·3%	15·6%	3·1%			12·5%
Cameroon	0·7% (0·5%-0·8%)	164 (117-184)				40·0%	20·0%		40·0%			

Region/ Country	Viremic Prevalence in 2015[i]	Viremic Population (000) in 2015[i]	Genotypes[ii]								
			1a	1b	1c	1 (Other)	2	3	4	5	6	Mixed/ Other
Chad	1·1% (0·8%-1·3%)	162 (111-184)				7·7%	7·7%		84·6%			
Gambia, The	0·8% (0·5%-1·3%)	17 (10-27)				19·4%	58·1%	6·5%				16·1%
Ghana	1·4% (1·1%-3·4%)	399 (305-944)	0·1%	0·2%		12·8%	87·0%					
Guinea-Bissau						1·8%	98·2%					
Nigeria	1·4% (1·0%-1·4%)	2,553 (1,902-2,651)				82·3%	5·9%	7·4%	4·4%			

[i] 2015 year-end estimate is a model output projection based on historic data
[ii] Genotype distribution data are either taken from the literature or based on regional averages in the absence of country-specific data

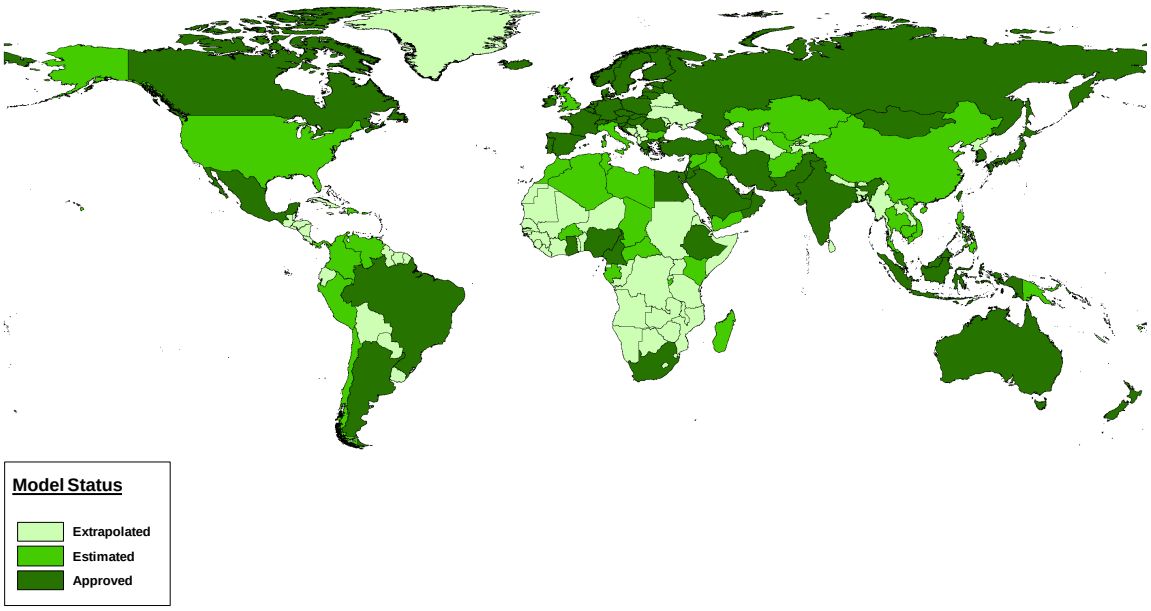
Table 2. Regional prevalence and number of infected individuals (all ages)

Regions	Viremic HCV Prevalence (95% UI)	Population (Millions)	Viremic HCV Infected (Millions) (95% UI)
Asia Pacific, High Income	0·6% (0·3%-0·7%)	183	1·1 (0·6-1·3)
Asia, Central	3·6% (2·8%-3·9%)	88	3·2 (2·5-3·4)
Asia, East	0·7% (0·5%-0·8%)	1,439	10·5 (7·3-11·6)
Asia, South	0·9% (0·7%-1·3%)	1,742	15·3 (12·3-22·7)
Asia, Southeast	0·7% (0·5%-0·8%)	654	4·7 (3·2-5·2)
Australasia	1·0% (0·8%-1·0%)	29	0·3 (0·2-0·3)
Caribbean	0·5% (0·4%-0·8%)	45	0·2 (0·2-0·4)
Europe, Central	1·0% (0·8%-1·0%)	118	1·2 (0·9-1·2)
Europe, Eastern	3·3% (2·1%-3·4%)	206	6·7 (4·2 -7·0)
Europe, Western	0·5% (0·4%-0·8%)	426	2·3 (1·9-3·2)
Latin America, Andean	0·5% (0·3%-0·6%)	59	0·3 (0·2-0·3)
Latin America, Central	0·5% (0·4%-0·5%)	247	1·3 (0·9-1·3)
Latin America, Southern	0·6% (0·3%-0·9%)	64	0·4 (0·2-0·6)
Latin America, Tropical	0·9% (0·6%-0·9%)	211	1·8 (1·3-2·0)
North Africa/Middle East	1·7% (1·4%-1·9%)	498	8·5 (6·8-9·2)
North America, High Income	0·9% (0·7%-1·1%)	362	3·2 (2·4-4·0)
Oceania	1·1% (0·8%-3·7%)	11	0·1 (0·1-0·4)
Sub-Saharan Africa, Central	2·1% (0·1%-6·9%)	115	2·4 (0·1-8·0)
Sub-Saharan Africa, East	0·5% (0·4%-0·7%)	425	2·1 (1·6-2·9)
Sub-Saharan Africa, Southern	0·7% (0·4%-0·9%)	76	0·5 (0·3-0·7)
Sub-Saharan Africa, West	1·3% (1·1%-1·4%)	399	5·1 (4·3-5·7)
Total	1·0% (0·8%-1·1%)	7,397	71·1 (62·5-79·4)

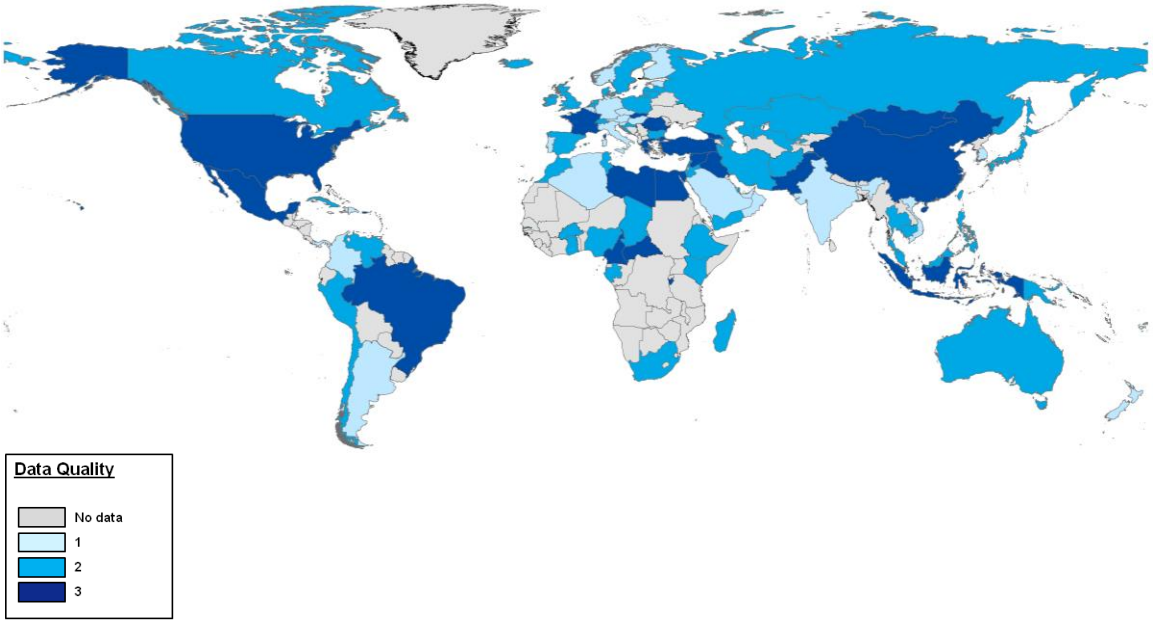
Figures

Figure 1. Evolution of country HCV prevalence estimates (end of 2015)

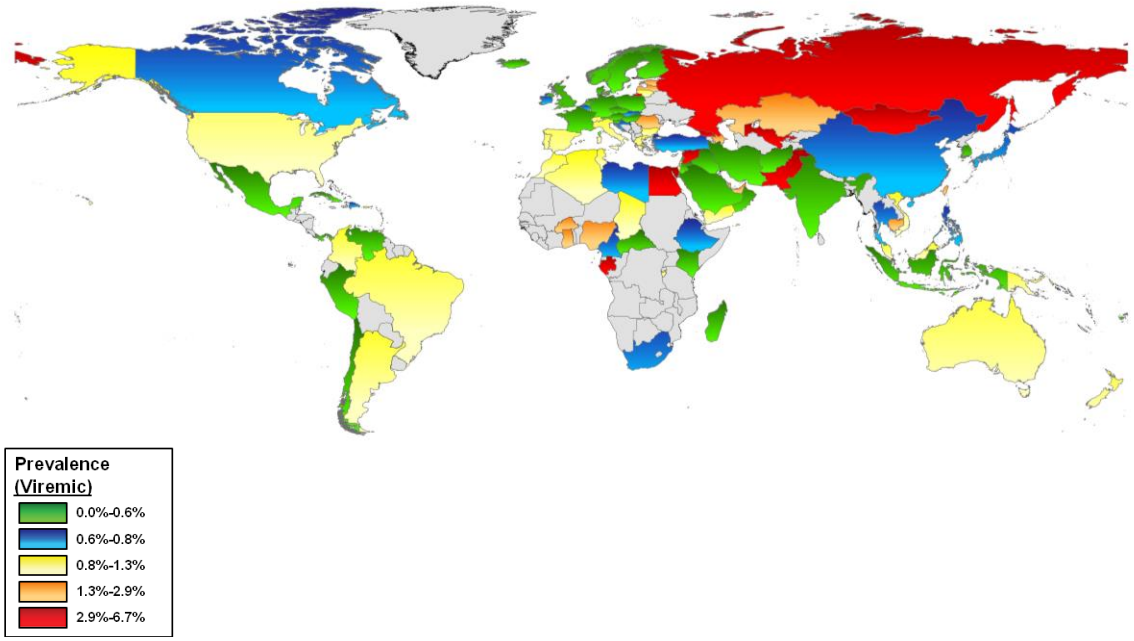
A. Countries with approved and estimated models and extrapolated prevalence



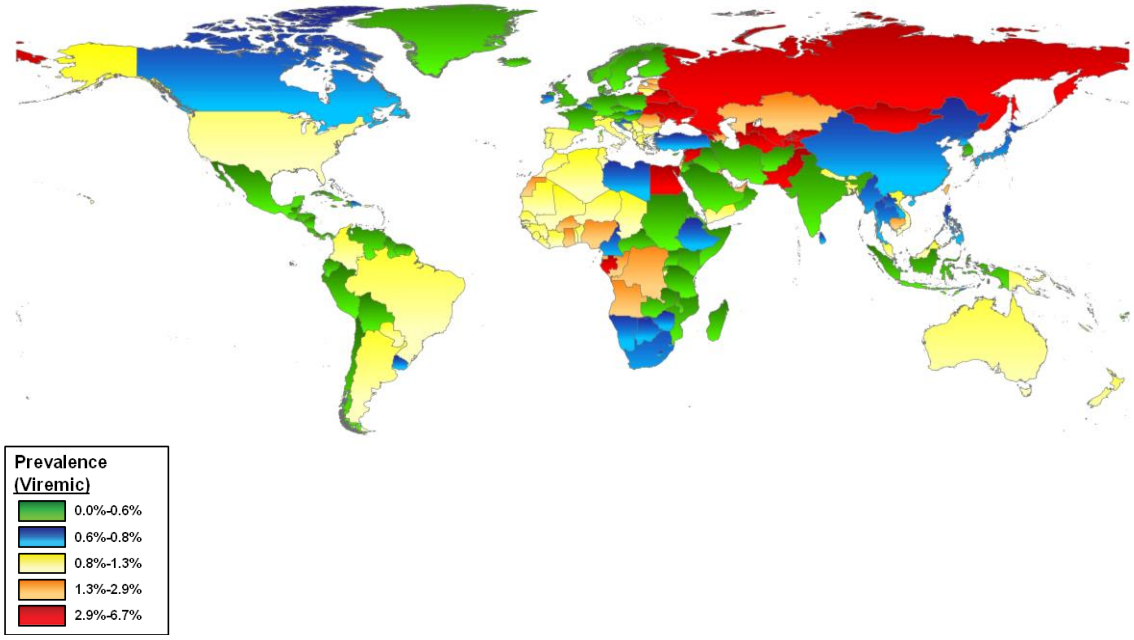
B. Data quality among countries with approved or estimated models



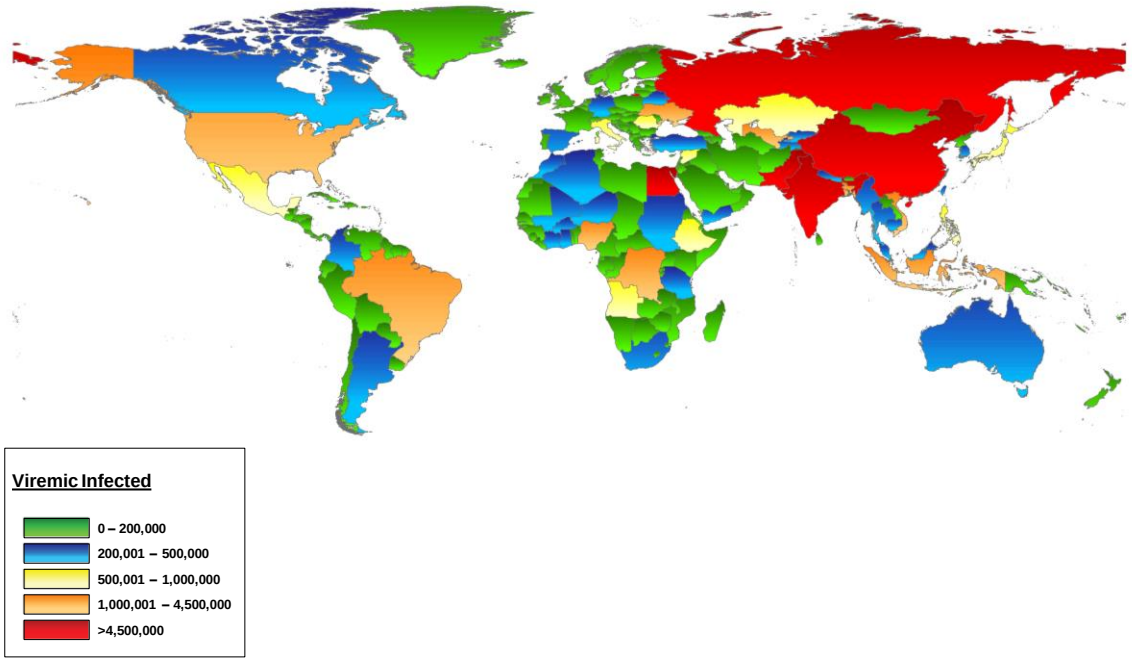
C. 2015 Viremic prevalence among countries with approved or estimated models



D. Viremic prevalence all countries



E. Number of viremic infected all countries



F. HCV genotype and total infected by GBD region

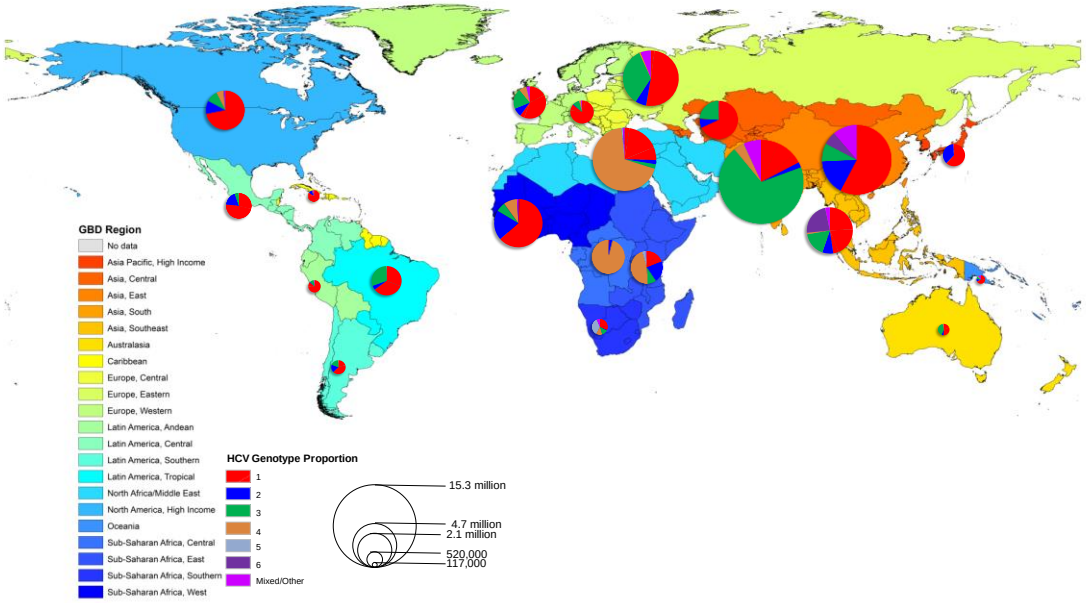


Figure 2. Countries accounting for 80% of the total viremic HCV infections

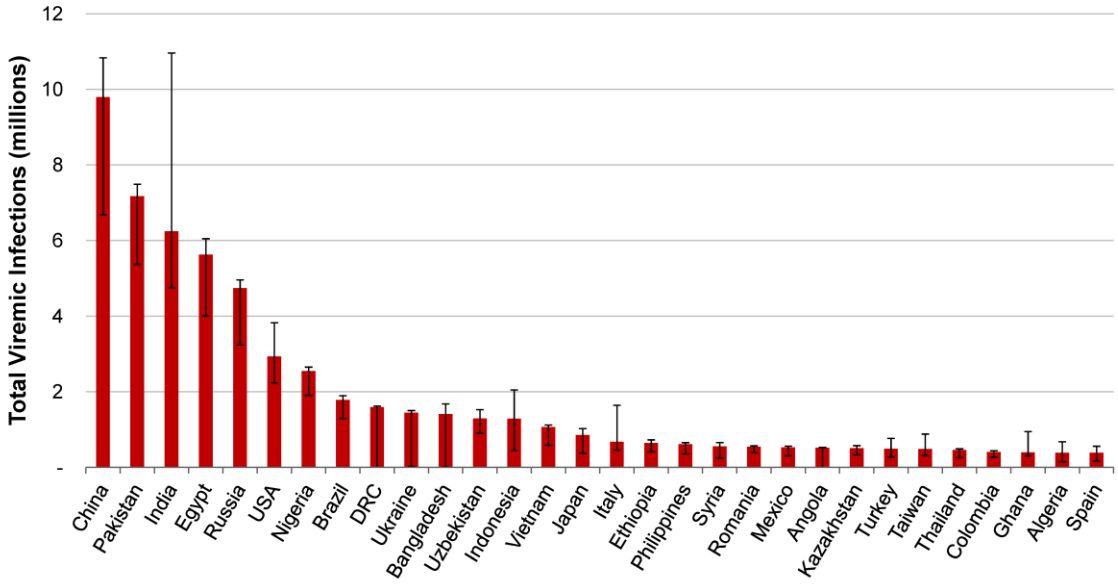


Figure 3. Sensitivity analysis of global viremic infections – all ages (top 10)

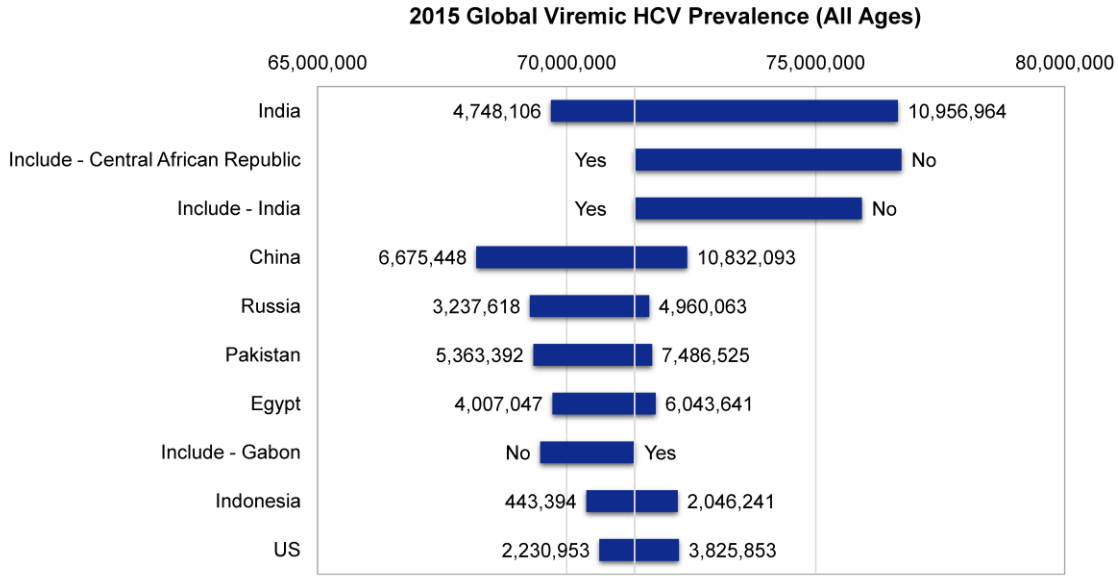


Figure 4. Genotype distribution by GBD region

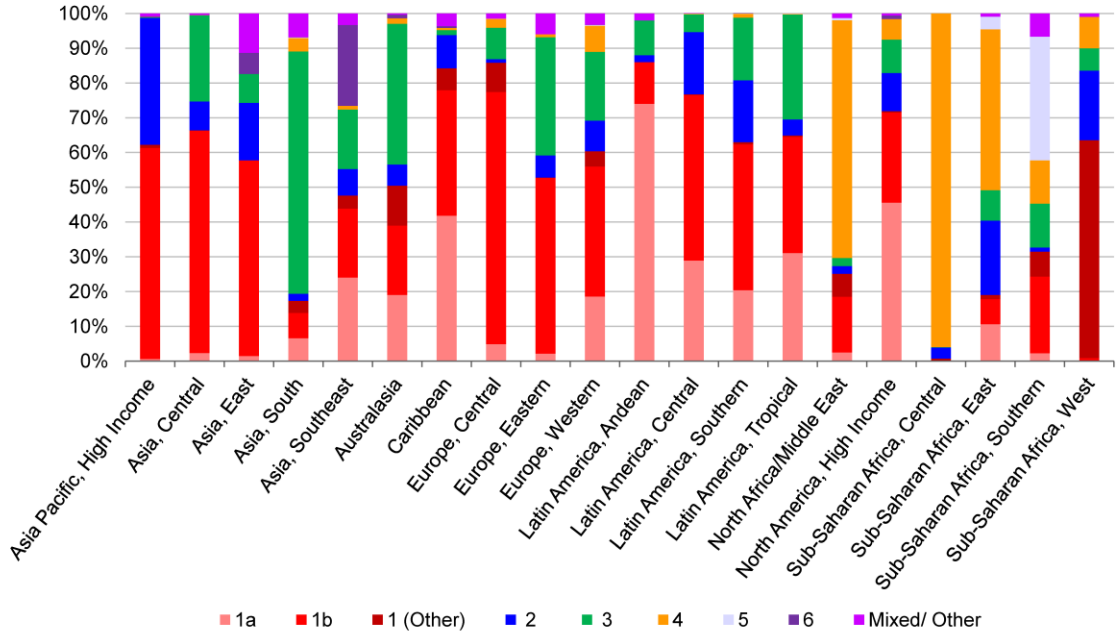


Figure 5. Comparison of this and previous HCV prevalence estimates

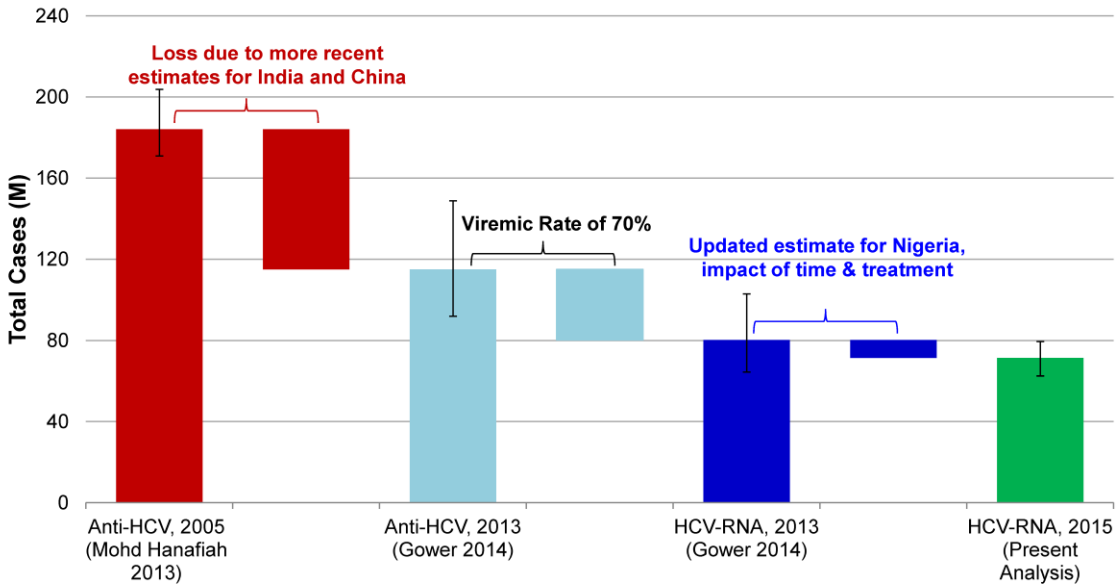
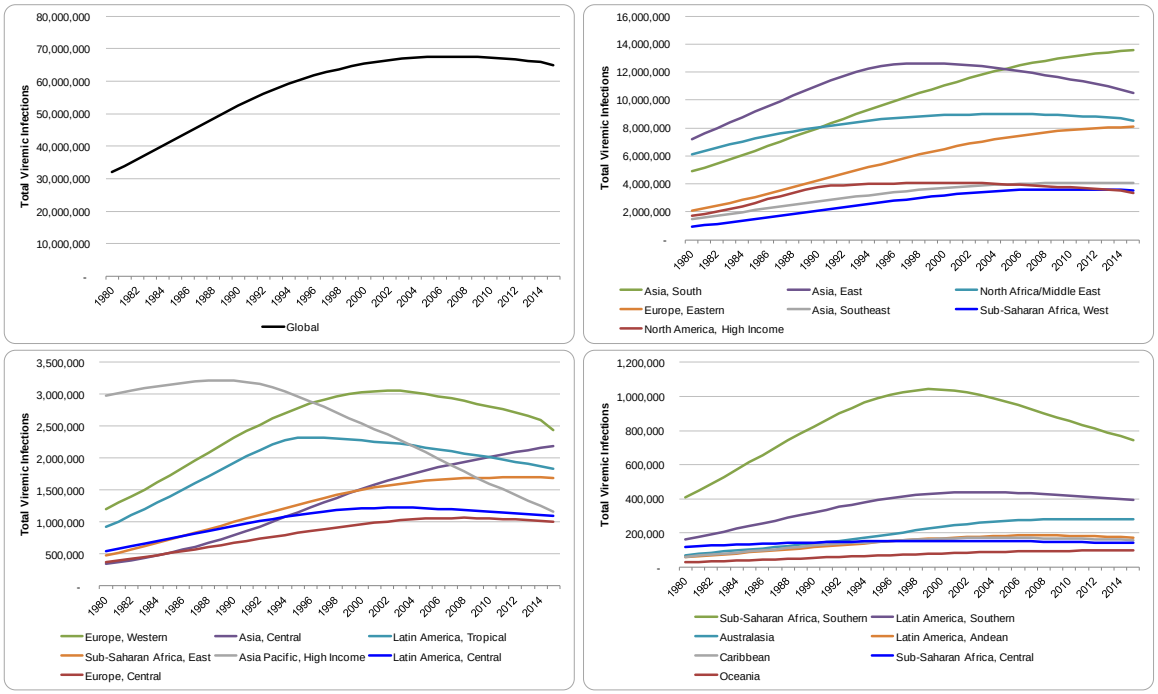


Figure 6. Change in viremic HCV prevalence by GBD Region



1 Evolution of country HCV prevalence estimates (end of 2015)

2 Countries accounting for 80% of the total viremic HCV infections

3 Sensitivity analysis of global viremic infections – all ages (top 10)

4 Genotype distribution by GBD region

5 Comparison of this and previous HCV prevalence estimates

6 Change in viremic HCV prevalence by GBD Region