Web Annex B. WHO estimates of the prevalence and incidence of hepatitis C virus infection by WHO region, 2015

Centre for Disease Analysis

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The named institution alone is responsible for the views expressed in this publication.

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WHO estimates of the prevalence and incidence of HCV infection by regions, 2015

Online annex # 3 to the 2017 WHO Global Hepatitis Report on the cascade of care – Version: 20 April 2017

Background

Since 2000, global public health stakeholders have increasingly recognized viral hepatitis as a major cause of death. In 2015, WHO's Global Health Estimates [GHE] indicated that acute liver failure, cirrhosis and hepatocellular carcinoma secondary to viral hepatitis lead to more deaths worldwide than the human immunodeficiency virus [HIV], tuberculosis [TB] or malaria (1). In addition, unlike malaria, HIV or TB, mortality trends for hepatitis have been increasing (1). In May 2016, the World Health Assembly [WHA] approved a Global Health Sector Strategy [GHSS] on viral hepatitis, which calls for the elimination of hepatitis C virus [HCV] as a public health threat by 2030 (2). Specifically, the GHSS aims to achieve reductions in viral hepatitis related mortality (10% reduction by 2020 and 65% reduction by 2030) and new HBV and HCV infections (30% reduction by 2020 and 90% reduction by 2030) (2).

According to WHO, in 2015, 29.7% of hepatitis deaths were attributable to infection with HCV (1). These deaths in 2015 were secondary to infections acquired in the past. Current hepatitis-related mortality reflects on the consequences of transmission in the past. Mortality from late-stage chronic liver diseases from viral hepatitis, including decompensated cirrhosis and hepatocellular carcinoma, are difficult to prevent with treatment. However, future deaths due to current infections can be averted. Achieving sustained viral response [SVR] through the treatment of HCV infection has been associated with a reduction in mortality (all-cause and liver-related) (3). Testing and treatment offers an opportunity to improve survival among persons affected with prevalent infections while prevention can reduce incidence.

As WHO guides its member states in the implementation of the GHSS on viral hepatitis, baseline regional and global estimates of the prevalence and incidence of HCV infection are needed to (a) identify priorities for action and (b) compare regions in terms of incidence and prevalence. The objective of this analysis is to estimate the prevalence and incidence of HCV infection at the regional and global levels in 2015. According to the global monitoring and evaluation framework for hepatitis B and C (4), prevalence is an indicator of context (numbered C.1.b for HCV and C.1.a for HBV) that allows estimating needs and planning a response. While serological evidence of past or present HCV infection can be used to assess the annual risk of infection in a population, the prevalence of chronic infection is a more useful metric, since it estimates the proportion of the population that needs to be assessed for treatment. Incidence is an indicator of impact (numbered C.9.b for HCV and C.9.a for HBV) that can be used to evaluate prevention activities, including, also, the use of treatment as prevention (4).

Methods

General approach

To obtain global and regional estimates, we proceeded in four steps. First, we used published and unpublished data to generate country-level disease burden models along with a modified Delphi process to estimate incidence and prevalence of chronic HCV infections at the national level (

). Second, we used the estimates from countries with available data to compute regional and global estimates. Thus, for countries where data were insufficient to build a model, estimates from the same GBD region were used given the geographical proximity and epidemiological similarity to generate regional and global estimates. Third, we calculated uncertainty intervals around the estimates.

Operational definitions

We used definitions proposed in 2016 by WHO (4). We defined serological evidence of past and present infection by the absence of acute hepatitis and the presence of anti-HCV. We defined chronic HCV infection (for indicator C.1.b) as the absence of acute hepatitis and the presence of HCV RNA or HCV core antigen. We defined incidence of HCV infection (for indicator C.9.b) as the number of new infections with HCV in a year (to be divided by the population size to calculate a rate).

Time period

Our systematic search considered available published studies between January 1, 2000 and March 31, 2016. We modelled outcomes, including prevalence of HCV infection at the end of the year 2015 and incidence of HCV infection for the year 2015.

Geographical scope

We considered all countries for the construction of models but targeted countries with a total population of 1.5 million people or more to organize meetings of experts to review estimates.

1. Country-level estimates

General approach

The detailed methods for the national level estimates are described elsewhere (5-8). In summary, the Center for Disease Analysis (CDA) developed a country-level HCV infection model, which in 2016 was in its 39th iteration, to incorporate the most recent epidemiological assumptions and estimate prevalence and incidence. We performed a systematic search, and scored studies using a multi-objective decision analysis approach (5, 9-11).

Systematic search and quality scoring

Inclusion criteria

For all countries, we searched PubMed and EMBASE, for any publications that included data on prevalence of HCV infection published between January 1, 2000 and March 31, 2016. We included non-indexed government reports, personal communication with country experts, and additional studies identified through manual searches of references noted in publications when nationally representative studies were not available (Figure 1).

We included cross-sectional prevalence studies with a sample size of fewer than 1,000 if the study's prevalence estimate was within 5% of a previously cited estimate; if national experts confirmed during panel discussions that the study was the best available and most representative; and if the prevalence of infection was available by age and gender. We also made ad hoc inclusions detailed in the results and discussion.

Exclusion criteria

We excluded studies published prior to 2000, since first and second generation diagnostics lacked specificity (12). We also excluded studies conducted in groups that were not representative of the

general population (e.g., blood donors) or in high risk populations (e.g., people who inject drugs (PWID), minority ethnic groups, sex workers, refugees).

Quality scoring

We reviewed and scored studies that met the criteria. To limit the biases in data collection method, year of data collection, and sample size, we used a multi-objective decision analysis approach (Appendix 4) to generate a quality score on a scale of 1 (lowest) to 10 (highest) which were then clumped together into three categories (scale of 1 (lowest) to 3 (highest)) for simplicity. When multiple high-quality studies were available for a country, we modelled on the basis of the highest scoring study unless two national studies were available for different time-points in which case both were considered. A description of the high-quality studies excluded from the analysis is included in Appendix 5. We assigned modelling studies a quality score of 2 and expert consensus estimates a default score of 1, unless supportive data were available (Appendix 4). To provide an additional layer of validation, a second epidemiologist reviewed each study marked for inclusion to verify the scoring.

National Models

Markov models

We incorporated the epidemiological data obtained from the systematic search into a spreadsheet-based Markov model to forecast the prevalence and incidence of HCV infection. Since the prevalence of HCV infection changed over time, we modelled the size of the HCV-infected population from 1950 to 2015, accounting for incidence, disease progression, ageing, mortality, treatment and cure (6, 13).

Estimation of incidence

We developed curves of historical incidence by year based on reported estimates whenever possible. This methodology has previously been described in detail (8), while a summary is provided below.

When two prevalence studies with age and gender distribution were available, we used them to calculate the average number of incident infection by age between the two time points, taking into consideration background mortality, liver-related deaths, and the number of individuals treated and cured.

When reliable prevalence estimates were available at only one point in time, we used a similar methodology, but calculated the total number of incident infections occurring between 1950 and the year of known prevalence, assuming there were no infected survivors among those who acquired HCV prior to 1950. We considered background mortality, liver-related deaths, and the number of individuals treated and cured. We then distributed new infections annually by taking into account known risk factors and the start of blood screening in the country. For example, national experts considered that after 1950, in many counties, the incidence of HCV infection began to increase between the 1960s and 1970s, and then decreased in the 1990s as HCV screening tests became more used in blood transfusion centres. Incidence data on acute hepatitis C were also used to inform the incidence trends in the model. In countries with a long life expectancy and known sources of infection prior to 1950 (e.g., Japan), we made adjustments to the prevalent population in 1950 to account for cases who were still alive in 2015.

We then distributed the annual incident cases by age and gender and compared the modelled distribution to the reported distribution. An iterative process of modifying the distribution of cases by

year and by age was used to match the two curves and estimate the annual number of new infections by year.

We finally calculated the incidence of HCV infection in 2015 on the basis of the prevalence by using the last year of known incidence data and/or asking the country experts if the prevalence has increased, decreased or stayed the same since that time. In the absence of better information, we assumed the number of new infections per year would stay constant in the future.

In country review

Once we developed a model, we sought peer-review comments from national experts. We held meetings to get consensus around input variables and to validate the outputs against available empirical data (

Appendix 6). Once expert consensus was gained for a country, we considered the country model "approved". For countries with high-quality data where we were unable to hold expert panel meetings, we completed models on the basis of published literature alone. We then validated the model by comparing its output (e.g., incident cases of hepatocellular carcinoma) against empirical data (e.g., reported incidence of hepatocellular carcinoma due to HCV infection) in countries with available data. In addition, a second, epidemiologist reviewed data inputs, model calibration, and outputs for consistency in methods, before being included into the global, regional, and income group estimates.

2. Extrapolations to generate regional estimates

To develop regional and global estimates, we aggregated model outputs from countries to generate estimates by GBD regions using weighted averages, extrapolated the GBD regional prevalence to countries without data and summed all country-level estimates (modelled and extrapolated) to generate a global estimate.

GBD regional estimates for countries with data

We estimated the GBD regional prevalence and incidence as the population-weighted average of the number of incident and prevalent infections from the country-level models. We assigned countries, territories and areas without a formal GBD designation based on WHO region and geographical proximity.

GBD extrapolations to countries without data

We used GBD regional prevalence and incidence rates as estimates for countries without models.

Global and regional estimates

Once each country had a prevalence and incidence estimate (modelled or extrapolated), we compiled cases and divided them by the global population to estimate prevalence and incidence by WHO region, income groups and for the world.

3. Uncertainty and sensitivity analyses

We conducted a sensitivity analysis and developed 95% uncertainty intervals (UI) at both stages of the analysis (country-level and regional/global). We captured country-level uncertainty using ranges around model input data including prevalence, disease progression and mortality rates (Appendix 1, Appendix 3) (8). To do this, we run a Monte Carlo uncertainty analysis that randomly sampled values from within the range of each input to then calculate the uncertainty range around outputs (in this case, prevalence and incidence). After completion of the Monte Carlo analysis, we exported the resulting uncertainty ranges by country for calculations at the regional and global level.

We then ran a Monte Carlo analysis on the country ranges, assuming that all countries were independent from one another (for example, a higher prevalence in Belgium was assumed to be independent from a higher prevalence in Spain). Countries without data were set equal to the "known" regional prevalence (a live calculation that summed the data from known countries within the region). As the Monte Carlo analysis ran, the prevalence in countries without data changed whenever the "known" regional prevalence changed, thus magnifying the uncertainty to account for countries without data.

In addition, we ran a sensitivity analysis to turn off and on the inclusion of each country in the overall global estimate. This allowed us to determine the impact of including each country's forecast in the

regional prevalence estimate, which in turn determined the estimated prevalence for all countries with missing data in the same region. We conducted these analyses using Crystal Ball®, an Excel® add-in by Oracle® with a binomial distribution to include or exclude countries, and Beta-PERT distributions for all uncertain inputs (14).

Results

Inclusion criteria allowed us to gather data to build 100 country models. Of those, 59 were approved by country experts. Combined, approved and estimated models captured 86% of the global population; accounting for 90-99% of the Western Pacific [WPR], Eastern Mediterranean [EMR], and Americas [AMR] regions, non-WHO-member countries; 85-89% of the South East Asian Region [SEAR] and European Region [EUR]; and 56% in the African Region [AFR].

Inclusions and exclusions

Following our protocol, we included nine studies with a sample size of fewer than 1,000. We included studies from four countries (Chile, Cuba, Jordan and Nigeria) after discussion with national experts (15, 16). The rationales for inclusion of these studies included: well designed study; sample size calculated to achieve statistical power given the population and assumed prevalence; and ministry of health sanctioned study. Two studies in Cambodia, both with sample size less than 1,000, were considered together because one was conducted in adults and one in children (17, 18). A study in Oceania was included for Fiji and Papua New Guinea because it had enough information to provide the distribution of HCV infections by age (19). In Kazakhstan, we included a cross-sectional study reporting prevalence of HCV infection by age because it was corroborated by a dataset of immigrants to Israel that had been considered in our previous analyses (3.2% vs. 3.3% anti-HCV) (20-22). Finally, in Uzbekistan, we included a study with a sample size of 929 because the small sample only occurred after the estimate was adjusted to remove blood donors (23).

We made two other inclusions that were not initially planned by our protocol. In Belgium, we included a study published prior to 2000, after deliberation with the expert panel (24, 25). This study, reporting serological evidence of past or present infection in 0.87% of the sampled population, was chosen over more recent estimates because it was deemed to have the most representative sampling and also fell within the range of the more recent studies (0.12% and 1.23% anti-HCV) and was deemed to have the most representative sampling (24, 26-28). Although the model allows for the inclusion of multiple studies from different time points, the newer studies were not scored sufficiently high to be included. In India, we used a meta-analysis by region, rather than a single study, to account for the various population sizes and prevalence estimates available (29). This inclusion came at the request of the expert panel, who pointed out that a majority of studies from India originated from the Punjab region (which has a high prevalence of HCV infection), and that this region accounted for only 2% of India's population.

Serological evidence of past or present HCV infection

Overall, 100.5 (95% UI: 88.6-109.5) million persons worldwide (1.4%, 95% UI: 1.2-1.5) had serological evidence of past or present HCV infection (Table 1). Prevalence was highest in EMR (3.0%, 95% UI: 2.5-3.1) for 19.9 million cases (95% UI: 16.5 – 20), and lowest in the SEAR (0.7%, 95% UI: 0.5-1.1) and AMR (0.9%, 95% UI: 0.7-0.9, Table 1) regions. With respect to income group, serological evidence of past or present HCV infection was highest in the lower-middle income [LMIC] group (1.6%, 95% UI: 1.4-1.8, 46 million individuals).

Chronic HCV infection

Overall, 71.1 (95% UI: 62.1-79.0 million) persons worldwide (1.0%, 95% UI: 0.8-1.1) had chronic HCV infection (Table 1). The prevalence of chronic HCV infection was highest in EMR (2.3%, 95% UI: 2.5-3.1), for 15.2 million cases (95% UI: 12.6-15.5, Table 1). However, the high prevalence in SEARO reflected a heterogeneous situation, with high prevalence in two countries and others with much lover prevalence. The lowest prevalence (0.5%, 95% UI: 0.4-0.9) was in SEAR. However, since SEAR had the largest regional population, the number of total cases was the fourth largest (10.4 million cases, 95% UI: 8.0-17.8, Table 1). The smallest number of total cases was in the AMR (0.7%, 95% UI: 0.6-0.8%, for 7.2 million cases, 95% UI: 6.1-8.0). When stratifying by income, prevalence of chronic infection, ranged from 0.8% (95% UI: 0.6-0.8) in the upper middle income [UMIC] group to 1.1% (95% UI: 1.0-1.3) in the LMIC group. The largest number of chronic cases was in the LMIC group (33.3, 95% UI: 28.7-38.0 million cases) and the smallest number of cases was in the low income [LIC] group (5.8, 95% UI: 3.8-10.1 million cases).

Proportion of infection among those with serological evidence of past or present HCV infection

The proportion of viraemic persons among those with past or present infection varied from 60 to over 80% by region and income group (Table 1). The AMR region and high income group had the highest proportion (84% and 76%), respectively. Of the 100 (95% UI: 88.6-109.5) million total persons with serological evidence of past or present infection with HCV, 71% were chronically infected.

Incidence of HCV infection

Globally, there were 1.7 (95% UI: 1.6-2.1) million incident cases of HCV infection in 2015, corresponding to an incidence rate of 23.7 (95% UI: 21.3-28.7) per 100,000 (Table 2). The highest incidence rates were in the EMR (62.5 per 100,000, 95% UI: 55.6-65.2, for 409,000 cases, 95% UI: 363,000-426,000) and EUR regions (61.8 per 100,000, 95% UI: 50.3-66.0, for 565,000 cases, 95% UI: 460,000-603,000). WPR had the lowest incidence rate (6.0 per 100,000; 95% UI: 5.6-6.6). However, AMR had the lowest total number of incident cases of HCV infection (63,000, 95% UI: 59,000-69,000).

With respect to income groups, the UMIC group had the lowest incidence rate (9.1 per 100,000; 95% UI: 7.6-11.4, Table 2), yet the total number of incident cases was lowest in the LIC Group (168,000, 95% UI: 104,000-340,000). The LMIC group reported the highest total number of incident cases (975,000, 95% UI: 862,000-1.2 million), for an incidence rate of 33.1 per 100,000 (95% UI: 29.3-40.3).

Results of the sensitivity analysis

Of the global estimates, SEAR, AFR, and WPR accounted for approximately 90% of variation within the model (Figure 5). If the total number of infections in SEAR was 14.4 million, rather than 10.4 million, the total number of infections globally would have been approximately 75.1 million cases, rather than 71.1 million. However, when considering incident HCV cases, the AFR region had the largest impact on uncertainty, accounting for more than 50% of the variation in estimates. WPR and AMR regions accounted for less than 1% of incident cases globally. By World Bank region, the LMIC and LIC groups accounted for more than 80% of uncertainty in the model.

India and China had the largest impact on the uncertainty of global estimates of the prevalence of infection. India alone accounted for almost half of the variation within the model. India and China also contributed the largest uncertainty by region, accounting for 93% and 94% of variation within SEAR and WPR, respectively. In AFR, where low quality studies that resulted in wider uncertainty intervals,

Nigeria, Ghana, Burundi, and Gabon accounted for over 75% of variation in the regional estimate. In EMR, the majority of uncertainty was accounted for by Pakistan and Egypt, which were responsible for over 95% of variation within forecasts. In EUR, Russia, Italy, and Uzbekistan accounted for more than 90% of variation, while the US contributes more than 75% of uncertainty within AMR.

India and Russia had the largest impact on the uncertainty of global incident cases in the forecast. In AFR, ten countries accounted for over 98% of variation in the model, with Ghana, Burundi, and Nigeria contributing more than half of the regional variation. In EMR, Pakistan, Egypt, and Syria had the largest impact (over 95%) on the uncertainty of regional estimates of prevalence of infection. In EUR, Russia and Uzbekistan accounted for more than 97% of variation; while in AMR, the United States accounted for more than half. India further accounted for 96% of variation in estimates within SEAR, while China and Vietnam accounted for 68% within WPR incident cases.

Of high income countries, Russia and Italy had the largest impact on variation (93%) within the model. In the UMIC group, Algeria, China, South Africa, Turkey and Iran accounted for more than 75% of uncertainty; while in the LMIC group, India and Pakistan accounted for the majority of variation. Lastly, of the LIC group, over 80% of variation was accounted for by ranges in Burundi, Ethiopia, and Gabon.

Evaluation of the model

For this analysis, we used a model that has undergone 39 iterations since it was first developed in 2011. We validated our first model for the United States using survey data from the National Health and Examination Survey against hepatocellular carcinoma data from the Surveillance, Epidemiology and End Results (SEER) Program database after adjusting for the proportion of hepatocellular carcinoma attributed to HCV infection (7, 30, 31). While our model for the US correctly predicted HCV-attributable hepatocellular carcinoma in a single year (compared with the adjusted SEER data), we found discrepancies in the trend of HCV-attributable HCC over time. After discussions with modelling specialists from Canada, the United Kingdom and France, we refined our progression rates by age, gender and METAVIR fibrosis stage (32). Following this update, both trend and point-estimated HCV-attributable HCC could be validated for the US as well as for Sweden which has extensive data on its HCV infected population.

We continued to validate country models by comparing the outputs against empirical data. In the USA, France and Egypt, at least two robust prevalence studies (from different time points) were available for comparison. In Egypt, we found that the modelled outcomes, based on 2008 input data, were predictive of the 2015 Egyptian Health Issues Survey results (33). In addition, the incidence of HCC cases was available through Globocan (6, 36-39). We used studies that reported the proportion of all hepatocellular carcinoma cases due to HCV infection (11, 40-55) to adjust the reported number of hepatocellular carcinoma cases and compare them against the model output. On the basis of these specific in-country validations, we adjusted parameters and updated formulas and modified data processing systematically so that all country models could run according to validated, standardized calculations.

Discussion

This analysis represents both an update to and significant expansion of previous efforts to estimate the prevalence and incidence of HCV infection globally. Historically, the prevalence of HCV infection has been difficult to quantify due to its asymptomatic nature and relatively recent discovery (1989).

In 1997, the first global estimate was published as part of a review of the existing literature to date (34). Prior to this time, a scarcity of country-level research had prevented the development of global and regional estimates. Since 2010, several studies have made progressive steps toward generating a representative global prevalence estimate although gaps in country data persist, particularly in Africa). First, a 2010 estimate of serological evidence of past or present infection (prevalence of infection – 2.35%) was developed through the aggregation of country-level prevalence estimate, following a review of the available literature (35). In 2013, the Global Disease Burden, Injuries, and Risk Factors 2010 Study (GBD 2010) estimated the prevalence of serological evidence of past or present infection at the global and regional level using a systematic review and a meta-analysis with age pattern modelling, reporting a global 2005 prevalence of 2.8% (36). In 2014, we published a comprehensive review and a meta-analysis that served as the foundation for the present work (5). The 2014 study adjusted prevalence estimates sampled from adult populations to account for lower prevalence in children, and reported a significantly lower prevalence of serological evidence of past or present infection of 1.6% (5). It also calculated the proportion of chronic infections among those with serological evidence of past or present infection (Figure 3).

Methodological strength of the current approach

Historically, most investigators estimated the global prevalence of HCV infection by multiplying the reported prevalence proportion among adults at a country-level by the whole country population in the year of interest. The use of this method is primarily driven by a lack of reliable data by age. However, these methods have a number of consequences. First, studies reporting age-specific prevalence of HCV infection indicate that prevalence is higher in adults than children. It may plateau or continue to increase in the population over 60 years of age (33, 37, 38). Thus, applying a prevalence estimate from adults to the entire population over-estimates the total number of cases. This issue is more problematic in countries with a young population. Second, the year of interest for the formulation of the estimate does not always match the year during which the country-level data was generated. When a country-level prevalence generated in a given year is multiplied by the country population three years later (for example), there have been three years of disease progression and mortality that are unaccounted for, further inflating the prevalence estimate. In contrast to this approach, our model considered at all stages of the analysis the year during which the data was generated and the age of the infected population. We applied each country prevalence estimate to the age cohort of the study from which it came. We also extrapolated ages outside of the reported cohort (8). Additionally, the model can accommodate input data from multiple time points, optimizing use of the input data accounting for aging and disease progression over time. Overall, compared with other studies, our regional and global prevalence and incidence estimates are adjusted for age, and then modelled to include the impact of mortality and cure over time.

The engagement of country experts and our use of a consistent methodology for all countries modelled constitutes an additional strengths of our method. The engagement of country experts assured that we did not rely only on published studies. For example, in referenced publications for Germany and Switzerland, experts increased the published prevalence estimates to account for under-reporting of high risk populations in those studies. Throughout these discussions, care was taken to ensure that in all approved countries the estimates were based on the best available information. Finally, the consistency in our methods assures that results from all modelled countries can be compared.

Implication of the prevalence for testing and treatment

The prevalence of chronic HCV infection ranges from 0.5% (95% UI: 0.4-0.9) in WPR to 2.3% (95% UI: 1.9-2.4) in EMR. However, the number of cases by region is relatively similar for all regions except for AMR. Additionally, in two regions (EUR and WPR) the proportion of viraemic among those with past or present infection was lower than 70%. These two points (low proportion viraemic and low prevalence) are important considerations for the development of national screening strategies. A lower proportion of viraemia among those with serological evidence of past or present infection means that more persons positive for anti-HCV will need to be screened for serological evidence of past or present HCV infections in order to identify viraemic patients who need treatment. Additionally, the amount of resources necessary for case finding increases as the prevalence decreases, suggesting that a different effort may be necessary across regions. The WHO recommends that "HCV serology testing be offered to individuals who are part of a population with high HCV seroprevalence or who have a history of HCV risk exposure/behaviour" (39). In countries or regions where unsafe injection practices are common, the population deemed to be at high risk could include much of the general population (39).

Implication of the incidence for prevention

Regional variations of incidence have implications for country and regional prevention efforts. The incidence rates in EMR and EUR (62.5 per 100,000 and 61.8 per 100,000 respectively) are about twice as high as the next region (31.0 per 100,000 in AFR). Differences in terms of rates are not so large by income groups. However, in LMIC, an incidence rate of 33.1 per 100,000 combined with a large population size means that the number of new infections occurring annually (975,000, 95% UI: 862,000-1,187,000) is more than double that of high income countries (390,000, 95% UI: 364,000-423,000). A 2014 study reported that between 2000 and 2010, the number of HCV infections due to healthcare injections decreased 83% globally, with 158,000-315,000 new HCV infections in 2010 (40). Regions with the largest number of health care injection associated HCV infections were EMR, SEAR and WPR (40). Efforts in these regions to better understand the most common risk factors of disease may lead to more effective prevention efforts in reducing global incidence. Cross-regional analyses may lead to a better understanding of successful interventions.

How these results update previous results

Our modelling 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 (71.1, 95% UI: 62.5-79.4 million chronic HCV infections) which was still within the uncertainty intervals of our previous estimate (80.2, 95% UI: 64.4-102.9 million chronic HCV infections) (Figure 3) (5). The current estimate does report a more narrow uncertainty range as a result of the updated methodology and incorporating country interviews. Compared with previous estimates, the number of infections is lower due to the availability of updated, lower estimates in China, India and Nigeria (5, 36). Additionally, our analysis focused on chronic HCV infections, while previous analyses have only presented serological evidence of past or present infection (36). Due to an updated methodology, inclusion of new models, updated inputs, and treatment trends with DAAs, overall estimates of the global prevalence of HCV infection is lower than previously (5, 36).

Limitations and bias

We took steps to minimize the impact of potential biases on the global and regional estimates (6, 41). Availability and quality of data was the first limitation in the estimates, especially in Sub-Saharan Africa.

To reduce the impact of publication bias, we included unpublished data, ministry of health reports and non-indexed sources. To ensure only high quality studies were considered and to minimize data collection bias, we established and followed a standard methodology for scoring articles. Two epidemiologists reviewed the literature and scored the studies. Of the total 100 countries modelled, 59 were approved with country experts to identify pertinent unpublished data and confirm assumptions and outcomes. We trained facilitators to reduce the impact of confirmation, observer, and recall bias biases that can happen during these meetings. After each meeting, a note-taker provided feedback on potential areas for improvement in facilitation.

Empirical data on incidence were difficult to obtain to verify modelled estimates. While a few countries have prevalence of HCV infection at two points in time (including the United States, France and Egypt) the majority of countries studied did not. During conversations on incidence, our facilitators were trained to help country experts think through the various risk factors for transmission and also to evaluate assumptions that seemed inconsistent. As the project progressed, we began to identify trends that served as qualitative checks and balances for the modelling. For example, across all countries, experts agreed that incidence was increasing prior to blood screening (generally early- to mid- 1990s) and that incidence should decrease after blood screening. In some countries, however, this reduction was offset by other risk factors, such as injection drug use. The magnitude of these changes, however, is more uncertain. In most countries, all-cause and liver-related mortality exceeded new infections leading to a decrease in total infections over the same period.

We used a weighted average to generate regional estimates, which could be perceived as another limitation, as more weight is given to studies from large countries. In a previous analysis, we ran a sensitivity analysis where we turned off and on individual countries with data to see the impact on the regional and global estimates (8). In fact, more populous countries did show a greater impact on the regional prevalence. In this situation, however, a weighted average was deemed more appropriate than a straight average based on data quality (Appendix, Figure 1b). The countries with a higher population generally tended to have higher quality studies, while studies in smaller countries tended to have a smaller sample size and much more uncertainty. Thus, in a straight average method, a low quality study in small country would have the same weight as a high quality study in a large country. To address the limitation of using a weighted average, the overall uncertainty intervals we present in this analysis include turning off and on all countries with data to ensure all sources of uncertainty associated with using the weighted average are accounted for.

The use of a model to forecast 2015 prevalence of HCV infection introduced another limitation – the accuracy of the model. When available, the outputs of the model were validated against empirical data, such as number of cases of hepatocellular carcinoma, to improve the accuracy of the modelling. However, a final limitation was the uncertainty in this empirical data. Two recent studies in Sweden and Melbourne, Australia demonstrate that HCC cases are under-reported by 37-50% (42, 43). This would result in an underestimation of HCC cases by our models.

Conclusions

HCV infection affects one percent of the world population. Regional hotspots for new and total cases require particular attention. A 2.3% prevalence of chronic HCV infections, compounded with a 62.5 per 100,000 incidence rate in EMR suggests a need for measures to both prevent new infections and address the current and potentially growing burden of advancing disease, Lower middle income

countries face a disproportionately high HCV challenge, accounting for the largest number of incident and prevalent cases. There is a gap in terms of biomarker surveys to inform incidence calculations in countries with outdated estimates.

Recommendations

Scaling up testing and treatment in high prevalence regions is necessary to prevent the progression of HCV to advanced liver disease and death. In regions of ongoing transmission, the sources of transmission must be identified through surveillance of acute hepatitis so that appropriate measures can be taken to reduce risk. This may include improvements in facility-level injection safety (Monitoring and evaluation core outcome indicator C.4.) or increased provision of sterile needles/syringes to persons who inject drugs (Monitoring and evaluation core outcome indicator C.5.). Finally, we recommend that biomarker surveys be conducted in countries or regions where data are scarce, and call on the scientific community for improved methods to estimate incidence reliably.

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Tables

Table 1: Prevalence (number and proportion) of serological evidence of past / present infection and HCV infection with uncertainty intervals, by region and income, 2015

	Region	2015 Population (Millions)	Serological evidence of past or present infection with HCV				Chronic HCV infections				Proportion of infections among those with past or present infection (%)
			Prevalence (%)		Total number (000)		Prevalence (%)		Total number (000)		
			Best estimate	Range	Best estimate	Range	Best estimate	Range	Best estimate	Range	
WHO Region	AMR	989	0.9	0.7 - 0.9	8,619	7,319 - 9,365	0.7	0.6 - 0.8	7,237	6,110 - 7,976	84
	AFR	1,000	1.5	1.1 - 2.2	14,657	11,292 - 21,714	1.0	0.7 - 1.6	10,284	7,271 - 15,878	70
	EMR	654	3.0	2.5 - 3.1	19,922	16,562 - 20,460	2.3	1.9 - 2.4	15,190	12,560 - 15,489	76
	EUR	914	2.3	1.8 - 2.4	20,935	16,759 - 21,814	1.5	1.2 - 1.5	13,641	10,901 - 14,151	65
	SEAR	1,945	0.7	0.5 - 1.1	13,414	10,590 - 22,143	0.5	0.4 - 0.9	10,391	8,019 - 17,826	77
	WPR	1,867	1.2	0.9 - 1.3	22,232	16,406 - 23,665	0.7	0.6 - 0.8	13,898	10,308 - 14,684	63
	Non-WHO	25	2.7	1.8 - 4.7	683	447 - 1,203	2.0	1.3 - 3.5	506	327 - 891	74
WB Income Group	High	1,408	1.3	1.1 - 1.4	17,817	15,299 - 19,226	1.0	0.8 - 1.0	13,499	11,578 - 14,682	76
	Upper middle	2,393	1.2	0.9 - 1.2	27,804	21,659 - 29,490	0.8	0.6 - 0.8	18,439	14,492 - 19,834	66
	Lower middle	2,946	1.6	1.4 - 1.8	45,929	39,992 - 52,751	1.1	1.0 - 1.3	33,341	28,683 - 38,986	73
	Low	644	1.4	1.0 – 2.2	8,881	6,572 - 14,288	0.9	0.6 – 1.6	5,846	3,804 - 10,093	66
	Other	3	1.1	1.0 - 1.4	31	28 - 40	0.7	0.6 - 0.8	20	18 - 23	66
	Global	**7,394**	**1.4**	**1.2 - 1.5**	**100,463**	**88,618 - 109,459**	**1.0**	**0.8 - 1.1**	**71,146**	**62,102 - 78,974**	**71**

Table 2: Incidence (number and rate) of HCV infection with uncertainty intervals, by region and income, 2015

	Region	2015 Population (Millions)	Incidence of HCV infection			
			Incidence Rate (per 100,000)		Total number (000)	
			Best estimate	Range	Best estimate	Range
WHO Region	AMR	989	6.4	5.9 - 7.0	63	59 - 69
	AFR	1,000	31.0	22.5 - 54.4	309	225 - 544
	EMR	654	62.5	55.6 - 65.2	409	363 - 426
	EUR	914	61.8	50.3 - 66.0	565	460 - 603
	SEAR	1,945	14.8	12.5 - 26.9	287	243 - 524
	WPR	1,867	6.0	5.6 - 6.6	111	104 - 124
	Non-WHO	25	22.9	19.4 - 42.4	6	5 - 11
WB Income Group	High	1,408	27.7	25.8 - 30.0	390	364 - 423
	Upper middle	2,393	9.1	7.6 - 11.4	218	183 - 273
	Lower middle	2,946	33.1	29.3 – 40.3	975	862 – 1,187
	Low	644	26.1	16.2 – 52.8	168	104 - 340
	Other	3	14.8	14.2 - 17.2	0.4	0.4 – 0.5
	Global	7,394	23.7	21.3 - 28.7	1,751	1,572 - 2,120

Figures

Figure 1: Process followed to (1) generate country models, (2) extrapolate regional estimates and (3) analyse uncertainty, HCV infection model, 2015

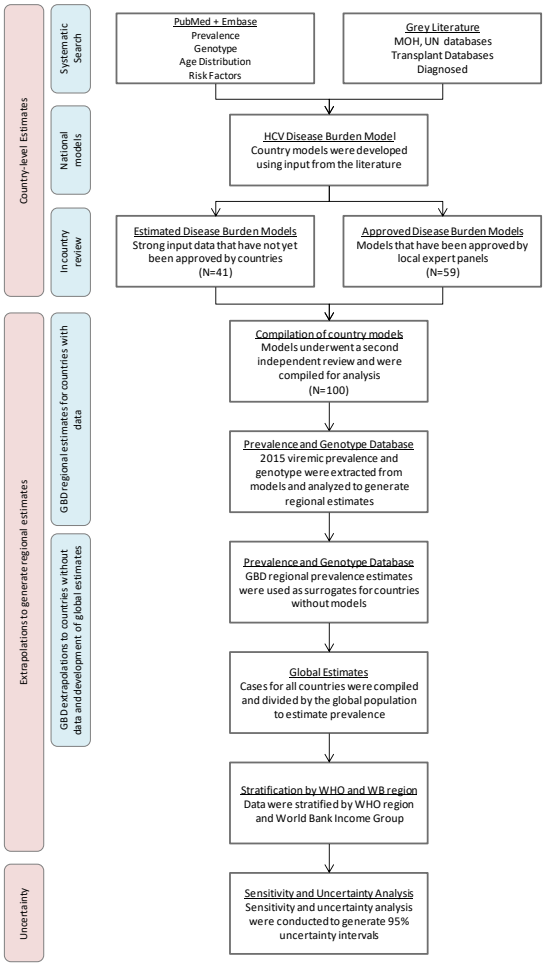


Figure 2: Distribution of prevalent and incident HCV infections, by region, 2015

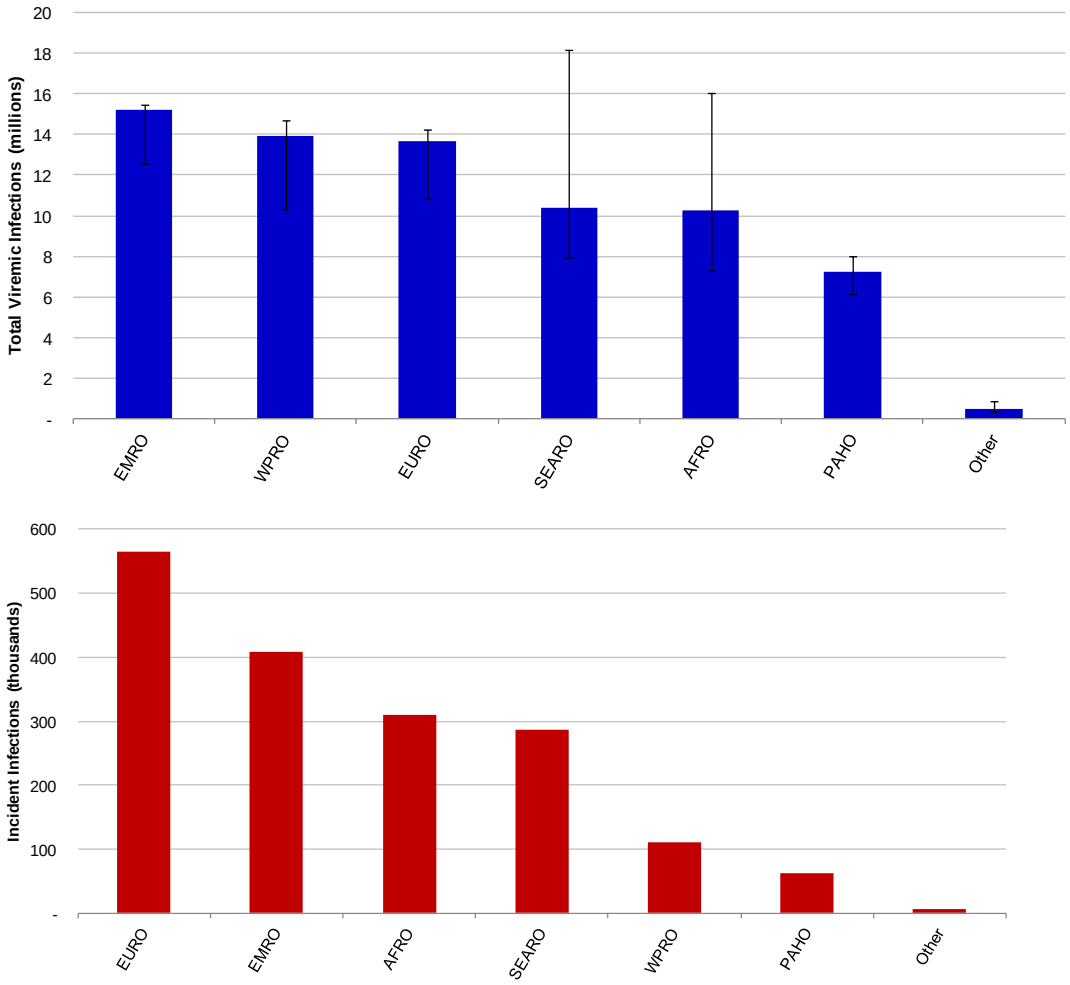


Figure 3: Changes in the estimate of prevalence of HCV infection

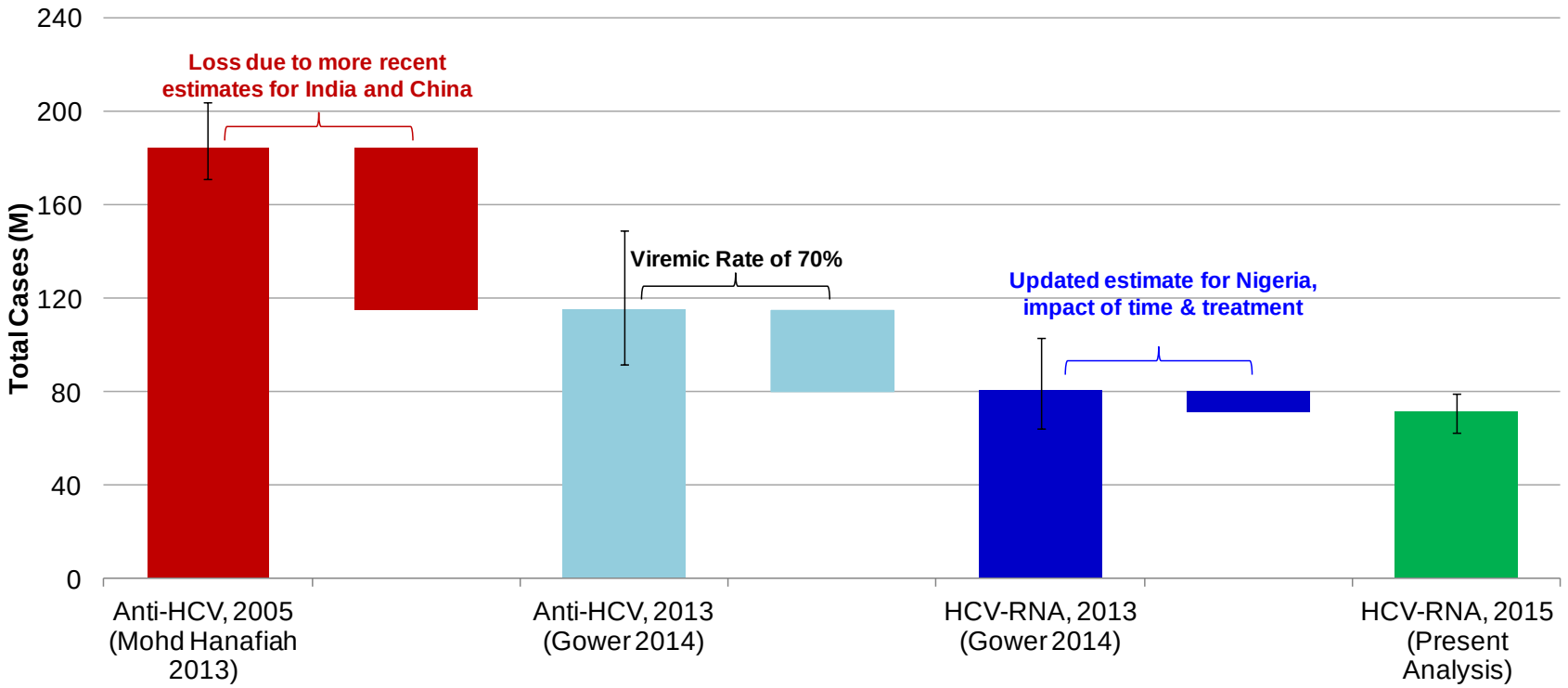
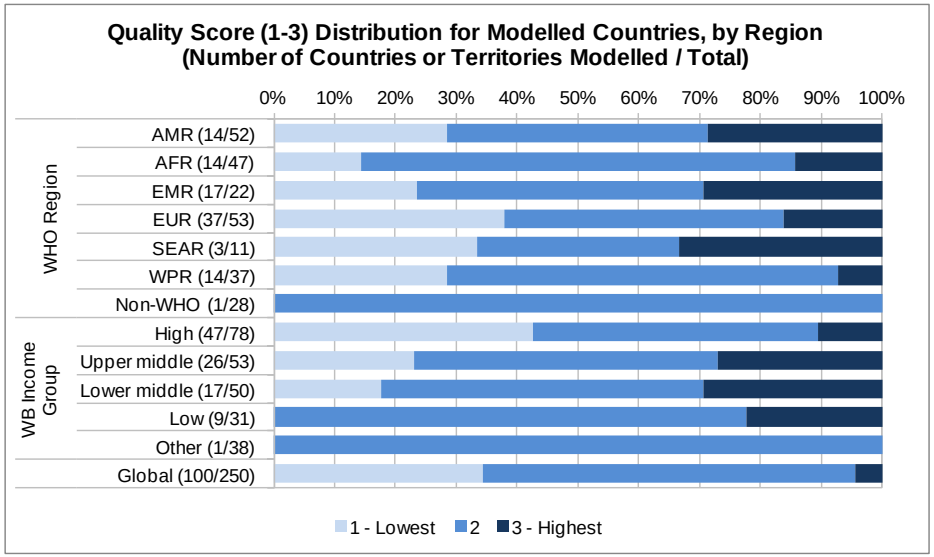


Figure 4: Quality of epidemiological data on HCV infection, by region



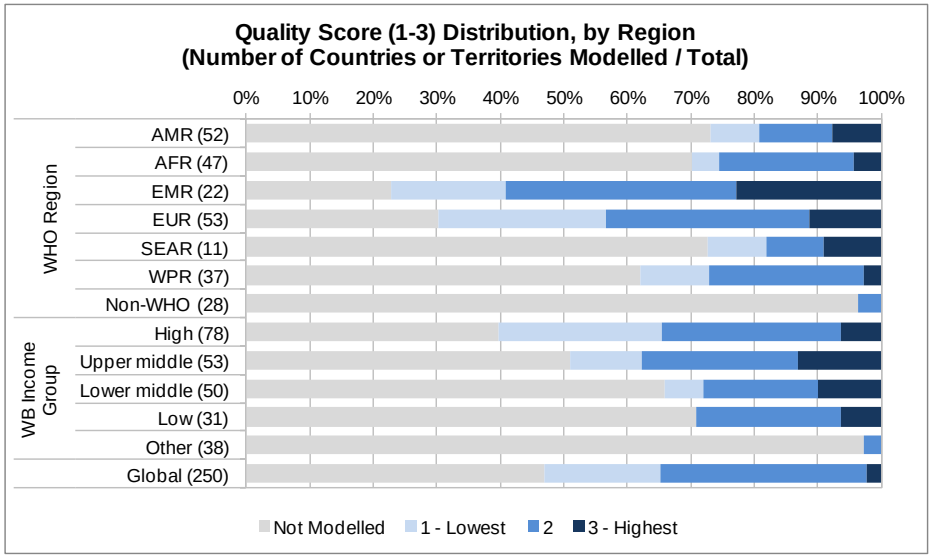
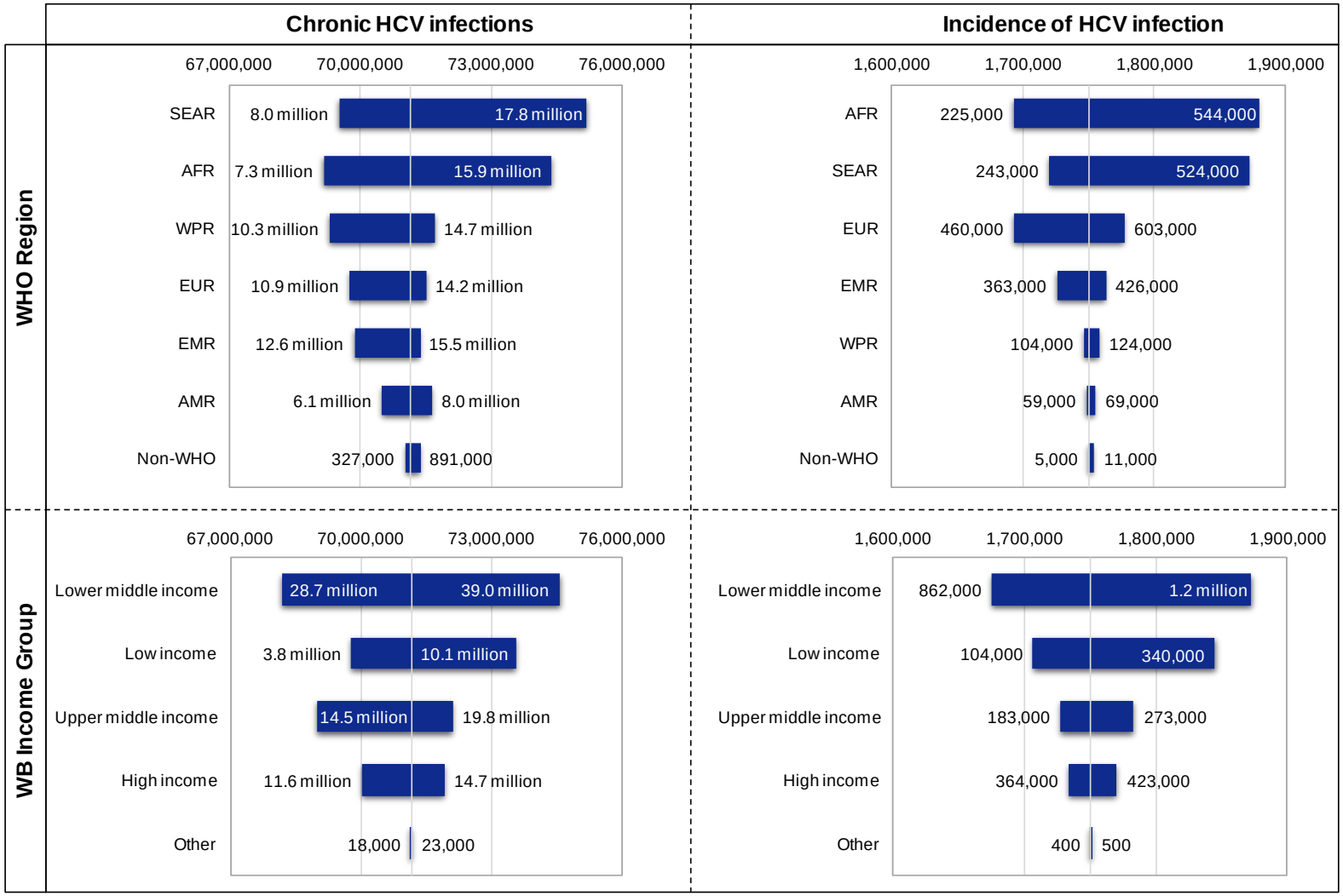


Figure 5: Sensitivity analysis to estimate the global prevalence and incidence of HCV infection, by region, 2015



References

Primary Sources

1. Global Health Estimates 2015: Deaths by Cause, Age, Sex, by Country and by Region, 2000-2015. [Internet]. 2016 [cited 02/21/2017]. Available from: http://www.who.int/healthinfo/global_burden_disease/en/.

2. Assembly WHOS-NWH. Global Health Sector Strategies Viral Hepatitis 2016-2021. 2016.

3. European Association for the Study of the Liver. Electronic address eee. EASL Recommendations on Treatment of Hepatitis C 2016. J Hepatol. 2016.

4. WHO. Monitoring and Evaluation for Viral Hepatitis B and C: Recommended Indicators and Framework. http://apps.who.int/iris/bitstream/10665/204790/1/9789241510288_eng.pdf: World Health Organization; 2016 Sep 30 2016.

5. Gower E, Estes C, Blach S, Razavi-Shearer K, Razavi H. Global epidemiology and genotype distribution of the hepatitis C virus infection. J Hepatol. 2014;61(1S):S45-S57.

6. Razavi H, Waked I, Sarrazin C, Myers RP, Idilman R, Calinas F, et al. The present and future disease burden of hepatitis C virus (HCV) infection with today's treatment paradigm. J Viral Hepat. 2014;21 Suppl 1:34-59.

7. Razavi H, Elkhoury AC, Elbasha E, Estes C, Pasini K, Poynard T, et al. Chronic hepatitis C virus (HCV) disease burden and cost in the United States. Hepatology. 2013;57(6):2164-70.

8. Blach S, Zeuzem S, Manns M, Altraif I, Duberg A-S, Muljono DH, et al. Global prevalence and genotype distribution of hepatitis C virus infection in 2015: a modelling study. The Lancet Gastroenterology & Hepatology.2(3):161-76.

9. Keeney RL, Raiffa H. Decisions with Multiple Objectives: Preferences and Value Tradeoffs: Cambridge University Press; 1993 1993.

10. Hammond JS, Keeney RL, Raiffa H. Smart Choices: A Practical Guide to Making Better Life Decisions. Boston, Massachusetts: Harvard Business School Press; 1999 1999.

11. Keeney RL. Value Focused Thinking: A Path to Creative Decisionmaking. Third Edition ed. Cambridge, Massachusetts: Harvard University Press; 1992 1992.

12. Technology WHO-DoBSaC. Hepatitis C Assays: Operational Characteristics - (Phase I) - Report 2 - July 2001. Geneva; 2001 7/2001.

13. Razavi H, Estes C, Pasini K, Gower E, Hindman S. HCV treatment rate in select European countries in 2004-2010. Journal of Hepatology. 2013;58:S22-S3.

14. Malcolm DG, Roseboom JH, Clark CE, Fazar W. Application of a Technique for Research and Development Program Evaluation. Operations Research. 1959;7(5):646-69.

15. Epidemiology Do. National Survey of Viral Hepatitis B and C Infection in Nigeria. Nigerian Center for Disease Control; 2013 November 2013.

16. Hamoudi W, Ali SA, Abdallat M, Estes CR, Razavi HA. HCV infection prevalence in a population recruited at health centers in Jordan. Journal of epidemiology and global health. 2013;3(2):67-71.

17. Yamada H, Fujimoto M, Svay S, Lim O, Hok S, Goto N, et al. Seroprevalence, genotypic distribution and potential risk factors of hepatitis B and C virus infections among adults in Siem Reap, Cambodia. Hepatology Research. 2015;45(4):480-7.

18. Fujimoto M, Yamada H, Akita T, Lim O, Hok S, Matuso J, et al. Study on hepatitis viral infection among school students in Cambodia. Hepatology International. 2013;7:S458.

19. Harrison GLA, Pryor J, Malani J, Supuri M, Masta A, Teriboriki B, et al. Infection Frequency of Hepatitis C Virus and IL28B Haplotypes in Papua New Guinea, Fiji, and Kiribati. PLoS ONE. 2013;8(8).

20. Nurgalieva ZZ, Hollinger FB, Graham DY, Zhangabylova S, Zhangabylov A. Epidemiology and transmission of hepatitis B and C viruses in Kazakhstan. World JGastroenterol. 2007;13(8):1204-7.

21. Zuckerman E. Hepatitis C in Israel. In: Razavi HA, editor. 2010.

22. Gower E, Estes C, Blach S, Razavi-Shearer KL, Razavi H. The global burden of viremic chronic HCV infection. Hepatology. 2014;60:914A.

23. Ruzibakiev R, Kato H, Ueda R, Yuldasheva N, Hegay T, Avazova D, et al. Risk factors and seroprevalence of hepatitis B virus, hepatitis C virus, and human immunodeficiency virus infection in uzbekistan. Intervirology. 2001;44(6):327-32.

24. Beutels M, Van Damme P, Aelvoet W, Desmyter J, Dondeyne F, Goilav C, et al. Prevalence of hepatitis A, B and C in the Flemish population. Eur J Epidemiol. 1997;13(3):275-80.

25. Van Damme P, Laleman W, Starkel P, van Vlierberghe H, Vandijck D, Hindman SJ, et al. Hepatitis C Epidemiology in Belgium. Acta Gastroenterol Belg. 2014;77(April-June):277-9.

26. Zanetti AR, Van Damme P, Shouval D. The global impact of vaccination against hepatitis B: a historical overview. Vaccine. 2008;26(49):6266-73.

28. Gerkens S, Martin N, Thiry N, Hulstaert F. [Hepatitis C: Screening and Prevention] HEPATITIS C: SCREENING EN PREVENTIE. 2012 2012.

30. Altekruse SF, Henley SJ, Cucinelli JE, McGlynn KA. Changing hepatocellular carcinoma incidence and liver cancer mortality rates in the United States. Am J Gastroenterol. 2014;109(4):542-53.

31. Surveillance, Epidemiology, and End Results (SEER) Program Research Data (1973-2013) [Internet]. National Cancer Institute. 2016 [cited August 10th 2016]. Available from: www.seer.cancer.gov.

32. Thein HH, Yi Q, Dore GJ, Krahn MD. Natural history of hepatitis C virus infection in HIV-infected individuals and the impact of HIV in the era of highly active antiretroviral therapy: a meta-analysis. AIDS. 2008;22(15):1979-91.

33. Ministry of Health and Population [Egypt], El-Zanaty and Associates [Egypt], ICF International. Egypt Health Issues Survey. Cairo, Egypt; 2015.

34. Hepatitis C: global prevalence. Wkly Epidemiol Rec. 1997;72(46):341-4.

35. Lavanchy D. Evolving epidemiology of hepatitis C virus. Clin Microbiol Infect. 2011;17(2):107-15.

36. Mohd Hanafiah K, Groeger J, Flaxman AD, Wiersma ST. Global epidemiology of hepatitis C virus infection: New estimates of age-specific antibody to HCV seroprevalence. Hepatology. 2013;57(4):1333-42.

37. Qureshi H, Bile KM, Jooma R, Alam SE, Afridi HU. Prevalence of hepatitis B and C viral infections in Pakistan: findings of a national survey appealing for effective prevention and control measures. East Mediterr Health J. 2010;16 Suppl:S15-23.

38. Ntagirabiri R, Baransaka E, Ndayiragije A, Niyongabo T. Prevalence of hepatitis C virus in Burundi: A nationwide survey. Journal Africain d'Hepato-Gastroenterologie. 2014;8(1):25-8.

39. WHO. Guidelines for the Screening, Care and Treatment of Persons with Chronic Hepatitis C Infection. Updated version, April 2016. http://www.who.int/hepatitis/publications/hepatitis-c-guidelines-2016/en/: World Health Organization; 2016 April 2016.

40. Pepin J, Abou Chakra CN, Pepin E, Nault V, Valiquette L. Evolution of the global burden of viral infections from unsafe medical injections, 2000-2010. PLoS One. 2014;9(6):e99677.

41. The Polaris Observatory HCV Collaborators, Blach S, Zeuzem S, Manns M, Altraif I, Duberg A, et al. Global prevalence and genotype distribution of hepatitis C virus infection in 2015: a modelling study. The Lancet Gastroenterology & Hepatology. 2016;Under Review.

42. Torner A, Stokkeland K, Svensson A, Dickman PW, Hultcrantz R, Montgomery S, et al. The underreporting of hepatocellular carcinoma to the cancer register and a log-linear model to estimate a more correct incidence. Hepatology. 2016.

43. Hong TP, Gow P, Fink M, Dev A, Roberts S, Nicoll A, et al. Novel population-based study finding higher than reported hepatocellular carcinoma incidence suggests an updated approach is needed. Hepatology. 2016;63(4):1205-12.

Appendix Sources

27. Quoilin S, Hutse V, Vandenberghe H, Claeys F, Verhaegen E, De Cock L, et al. A population-based prevalence study of hepatitis A, B and C virus using oral fluid in Flanders, Belgium. Eur J Epidemiol. 2007;22(3):195-202.

29. Saraswat V, Norris S, de Knegt RJ, Sanchez Avila JF, Sonderup M, Zuckerman E, et al. Historical epidemiology of hepatitis C virus (HCV) in select countries - volume 2. J Viral Hepat. 2015;22 Suppl 1:6-25.

44. Khan S, Attaullah S. Share of afghanistan populace in hepatitis B and hepatitis C infection's pool: Is it worthwhile? Virology Journal. 2011;8.

45. Chemaitelly H, Chaabna K, Abu-Raddad L. The epidemiology of hepatitis C virus in the Fertile Crescent: Systematic review and meta-analysis. Hepatology. 2015;62:1101A.

46. Todd CS, Nasir A, Stanekzai MR, Bautista CT, Botros BA, Scott PT, et al. HIV, hepatitis B, and hepatitis C prevalence and associated risk behaviors among female sex workers in three Afghan cities. AIDS. 2010;24(SUPPL. 2):S69-S75.

47. Nasir A, Todd CS, Stanekzai MR, Bautista CT, Botros BA, Scott PT, et al. Implications of hepatitis C viremia vs. antibody alone on transmission among male injecting drug users in three Afghan cities. Int J Infect Dis. 2011;15(3):e201-5.

48. Ezzikouri S, Pineau P, Benjelloun S. Hepatitis C virus infection in the Maghreb region. J Med Virol. 2013;85(9):1542-9.

49. Elzouki AN, Smeo MN, Sammud M, Elahmer O, Daw M, Furarah A, et al. Prevalence of hepatitis B and C virus infections and their related risk factors in Libya: A national seroepidemiological survey. Eastern Mediterranean Health Journal. 2013;19(7):589-99.

50. Coppola N, Zampino R, Bellini G, Macera M, Marrone A, Pisaturo M, et al. Cannabinoid receptor 2 (CB2) 63 QQ variant is associated with a severe histological activity index in patients with chronic hepatitis C. Journal of Hepatology. 2013;58:S183.

51. Fassio E, Schroder T. [Statement of the Argentinian Concensus on Hepatitis C 2007]. Acta Gastroenterol Latinoam. 2008;38(1):56-74.

52. Implante INCÚCdAe. El Sistema Nacional de Información de Procuración y Trasplante de la República Argentina 2014 [updated 2014. Available from: http://sintra.incucai.gov.ar/.

53. del Pino N, Oubina JR, Rodriguez-Frias F, Esteban JI, Buti M, Otero T, et al. Molecular epidemiology and putative origin of hepatitis C virus in random volunteers from Argentina. World J Gastroenterol. 2013;19(35):5813-27.

54. The Kirby Institute for Infection and Immunity in Society. HIV, viral hepatitis and sexually transmissible infections in Australia. Annual Surveillance Reports 1997-2013. 2013.

55. Bruggmann P, Berg T, Ovrehus AL, Moreno C, Brandao Mello CE, Roudot-Thoraval F, et al. Historical epidemiology of hepatitis C virus (HCV) in selected countries. J Viral Hepat. 2014;21 Suppl 1:5-33.

56. Australian Government Dept.of H, Ageing. National Notifiable Diseases Surveilllance System. Notifications of a selected disease by age group, sex and year: Hepatitis C (newly acquired) and Hepatitis C (unspecified): 1995-20132013.

57. Australian Government Department of Health and Ageing. National Notifiable Diseases Surveilllance System. Notifications of a selected disease by age group, sex and year: Hepatitis C (newly acquired) and Hepatitis C (unspecified): 1995-20152015.

58. Hope VD, Eramova I, Capurro D, Donoghoe MC. Prevalence and estimation of hepatitis B and C infections in the WHO European Region: A review of data focusing on the countries outside the European Union and the European Free Trade Association. Epidemiology and Infection. 2013;142(2):270-86.

59. Strauss R, Fulop G, Pfeifer C. Hepatitis C in Austria 1993-2000: reporting bias distort HCV epidemiology in Austria. Euro Surveill. 2003;8(5):113-8.

60. Mamedov MK, Alieva S. [Epidemiological characteristics and pathogenetical peculiaritries of subclinical infections caused with hepatitis B and C viruses among pregnant women living in Baku]. Georgian Med News. 2012(206):41-4.

61. Pimenov N.N CVP, Komarova S.V. et al. Hepatitis C in Russia: current epidemiology and approaches to improving diagnosis and surveillance. Epidemiology and Infectious Diseases. 2012;4:4-10.

62. Kurbanov F, Tanaka Y, Sugauchi F, Kato H, Ruzibakiev R, Zalyalieva M, et al. Hepatitis C virus molecular epidemiology in Uzbekistan. J Med Virol. 2003;69(3):367-75.

63. Daw MA, Dau AA. Hepatitis C virus in Arab world: a state of concern. ScientificWorldJournal. 2012;2012:719494.

64. Abdulla MAM, Al Qamish JRA. Hepatitis C Virus Infection: A Single Center Experience. Bahrain Medical Bulletin. 2008;30(1).

65. De Maeght S, Henrion J, Bourgeois N, de Galocsy C, Langlet P, Michielsen P, et al. A pilot observational survey of hepatitis C in Belgium. Acta Gastroenterol Belg. 2008;71(1):4-8.

66. Deltenre P, Moreno C, Mathurin P, Adler M, Louvet A, Castel H, et al. Impact of current treatment practice and different scenarios improving screening, access to treatment and treatment efficacy on HCV-related mortality in Belgium : A mathematical modeling approach. XXIIth BelgianWeek of Gastroenterology. 2010.

67. Pereira LM, Martelli CM, Moreira RC, Merchan-Hamman E, Stein AT, Cardoso MR, et al. Prevalence and risk factors of Hepatitis C virus infection in Brazil, 2005 through 2009: a cross-sectional study. BMC Infect Dis. 2013;13:60.

68. Surveillance MoH-BoH. [Epidemiological Bulletin of Viral Hepatitis] Boletim Epidemiológico Hepatites Virais Brasilia DF: Ministry of Health - Bureau of Health Surveillance - Department of STD, AIDS and Viral Hepatitis; 2012 [updated 2012. Available from: http://www.aids.gov.br/sites/default/files/anexos/publicacao/2012/51820/boletim_epidemiol_gico_hepatites_virais_2012_ve_12026.pdf.

69. Martins RM, Teles SA, Freitas NR, Motta-Castro AR, Souto FJ, Mussi A, et al. Distribution of hepatitis C virus genotypes among blood donors from mid-west region of Brazil. Rev Inst Med Trop Sao Paulo. 2006;48(1):53-5.

70. Güldem Ökem Z, Akgün S. White Paper - The Burden of Hepatitis C in CEE and CIS: An Epidemiological and Economic Assessment. 2009.

71. Mateva L, Antonov K, editors. Chronic hepatitis B and C in Bulgaria: why we need of screening? [PowerPoint slides]. World Hepatitis Day 2012; 2012; Sofia.

72. Teoharov P. Anti-HCV and HCV-RNA screening in Plovdiv region, 2010-2011. 2013.

73. Petrunov B, Kojauharova M, Teoharov P, Haidushka I, Sotirova P, Sredkova M, et al. EU project interreg II: seroepidemiology study on hepatitis C and B viral infections prevalence in Bulgaria and nothern Greece. Journal of Hepatology.36:138-9.

74. Meda Nea, editor Prevalence of Hepatitis B and C in the general population of Burkina Faso: Preliminary results from the ANRS 12270 Study. 8th International Meeting of the Francophone HIV/Hepatitis Health Alliance; 2016 2016 April 20 - 23; Brussels, Belgium: AFRAVIH 2016.

75. Layden J, Mora N, Phillips RO, Owusi-Ofori S, Sarfo FS, Kliethermes S, et al. High frequency of active HCV infection among seropositives in West Africa and evidence for multiple transmission pathways. Journal of Hepatology. 2015;62:S539-S40.

76. Coursaget P, Bourdil C, Kastally R, Yvonnet B, Rampanarivo Z, Chiron JP, et al. Prevalence of hepatitis C virus infection in Africa: Anti-HCV antibodies in the general population and in patients suffering from cirrhosis or primary liver cancer. Research in Virology. 1990;141(4):449-54.

77. O'Reilly JI, Ocama P, Opio CK, Alfred A, Paintsil E, Seremba E, et al. Risk factors and seroprevalence of hepatitis C among patients hospitalized at Mulago Hospital, Uganda. Journal of tropical medicine. 2011.

78. Akkarathamrongsin S, Praianantathavorn K, Hacharoen N, Theamboonlers A, Tangkijvanich P, Poovorawan Y. Seroprevalence and genotype of hepatitis C virus among immigrant workers from Cambodia and Myanmar in Thailand. Intervirology. 2011;54(1):10-6.

79. Ol HS, Bjoerkvoll B, Sothy S, Heng YV, Hoel H, Husebekk A, et al. Prevalence of hepatitis B and hepatitis C virus infections in potential blood donors in rural Cambodia. Southeast Asian Journal of Tropical Medicine and Public Health. 2009;40(5):963-71.

80. Njouom R. Prévalence de l'hépatite virale C au Cameroun : analyse des échantillons de l'Enquête Démographique de Santé 2011. In: Nde H, editor. 2015. p. 2.

81. Pasquier C, Njouom R, Ayouba A, Dubois M, Sartre MT, Vessiere A, et al. Distribution and heterogeneity of hepatitis C genotypes in hepatitis patients in Cameroon. J Med Virol. 2005;77(3):390-8.

82. Trubnikov M, Yan P, Archibald C. Estimated prevalence of Hepatitis C Virus infection in Canada, 2011. Canada Communicable Disease Report. 2014;40(19):429-36.

83. Public Health Agency of C. Hepatitis C in Canada: 2005-2010 surveillance report2012.

84. Seeff LB. Natural history of chronic hepatitis C. Hepatology. 2002;36(5 Suppl 1):S35-S46.

85. Ngaiganam Eea, editor Epidemiology of HBV, HCV and HDV in Central African Republic2016 2016 April 20 - 23; Brussels, Belgium: AFRAVIH 2016.

86. Njouom R, Frost E, Deslandes S, Mamadou-Yaya F, Labbe AC, Pouillot R, et al. Predominance of hepatitis C virus genotype 4 infection and rapid transmission between 1935 and 1965 in the Central African Republic. J Gen Virol. 2009;90(Pt 10):2452-6.

87. Bessimbaye N, Moussa AM, Mbanga D, Tidjani A, Mahamat SO, Ngawara MN, et al. [Seroprevalence of HBs Ag and of anti-HCV antibodies among HIV infected people in N'Djamena, Chad]. Bull Soc Pathol Exot. 2014;107(5):327-31.

88. Massenet D, Djime O. Seroprevalence of hepatitis C antiviral antibodies in blood donors in N'Djamena (Chad). Bulletin de la Société de pathologie exotique (1990). 1993;86(4):235.

89. Ali-Mahamat M, Njouom R. High rate of infection with hepatitis C virus genotype 4 in Chad, Central Africa. Indian Journal of Medical Microbiology. 2015;33(4):608-9.

90. Gonzalez R, Soza A, Hernandez V, Perez RM, Alvarez M, Morales A, et al. Incidence and prevalence of hepatitis C virus infection in Chile. Ann Hepatol. 2005;4(2):127-30.

91. Chile. Ministerio de Salud. [Clinical guide for the management of infection Hepatitis C virus] Guia clinica: manejo de la infeccion por virus de la hepatitis C (VHC). Santiago, Chile; 2010 2010.

92. Chen YS, Li L, Cui FQ, Xing WG, Wang L, Jia ZY, et al. [A sero-epidemiological study on hepatitis C in China]. Zhonghua liu xing bing xue za zhi = Zhonghua liuxingbingxue zazhi. 2011;32(9):888-91.

93. Fu Y, Wang Y, Xia W, Pybus OG, Qin W, Lu L, et al. New trends of HCV infection in China revealed by genetic analysis of viral sequences determined from first-time volunteer blood donors. J Viral Hepat. 2011;18(1):42-52.

94. Supply of blood for transfusion in Latin America and Caribbean countries 2012 and 2013. Washington, D.C.; 2015.

95. de la hoz FMD, M.E.; Pacheco Garcia, O.E..; Bonilla, H.Q.; Perez, N.T. Protocolo de Vigilancia en Salud Publica: Hepatitis B, C Y Coinfeccion Hepatitis B-Delta. 2014.

96. Vilibic-Cavlek T, Kucinar J, Ljubin-Sternak S, Kaic B, Lazaric-Stefanovic L, Kolaric B. Prevalence of viral hepatitis in Croatian adult population undergoing routine check-up, 2010-2011. Cent Eur J Public Health. 2014;22(1):29-33.

97. Martinez Campos JF, Perez Rodriguez A, Montalvo Villalba MC, Rodriguez Valdes K. Seroprevalencia y factores asociados a la hepatitis C en los municipios Playa y Marianao. Rev Panam Infectol. 2005;7(3):8-14.

98. Vigilancia de hepatitis B y C en Cuba [Powerpoint slides], Ministerio de Salud Publica de Cuba. Reunión sudamericana para una respuesta de salud pública a las hepatitis virales B y CMay 31, 2016.

99. Rodriguez Lay Lde L, Villalba MC, Corredor MB, Frometa SS, Hernandez JM, Carrera SD, et al. HCV genotype determination in monoinfected and HIV co-infected patients in Cuba. Trans R Soc Trop Med Hyg. 2012;106(12):711-7.

100. Nemecek V, Castkova J, Fritz P, Linhartova A, Svandova E, Sramova H, et al. The 2001 serological survey in the Czech Republic--viral hepatitis. CentEurJPublic Health. 2003;11 Suppl:S54-S61.

101. Christensen PB, Hay G, Jepsen P, Omland LH, Just SA, Krarup HB, et al. Hepatitis C prevalence in Denmark -an estimate based on multiple national registers. BMC Infect Dis. 2012;12:178.

102. Shichijo A, Mifune K, Aono H, Shibayama H, Terao H, Miyata A, et al. Seroepidemiological Studies of Hepatitis Viruses in the Dominican Republic: I. The Prevalence of Markers of Hepatitis A, B and C Viruses. Japanese Journal of Tropical Medicine and Hygiene. 1995;23(2):115-20.

103. Garcia V. Distribucion por edad y sexo [Powerpoint slides]. 2013.

104. Referencia Bd. Resultados de Salud Hepática: 2007-2014 [PowerPoint]. 2014 [Results from national screening program].

105. Liakina V, Hamid S, Tanaka J, Olafsson S, Sharara AI, Alavian SM, et al. Historical epidemiology of hepatitis C virus (HCV) in select countries – volume 3. Journal of Viral Hepatitis. 2015;22:4-20.

106. Board EH. Registered new cases of select communicable diseases and incidence rate per 100 000 inhabitants by gender and age group. 2014 5/12/2014. Report No.: NH02.

107. Ayele W, Nokes DJ, Abebe A, Messele T, Dejene A, Enquselassie F, et al. Higher prevalence of anti-HCV antibodies among HIV-positive compared to HIV-negative inhabitants of Addis Ababa, Ethiopia. J Med Virol. 2002;68(1):12-7.

108. Harrison GL, Pryor J, Malani J, Supuri M, Masta A, Teriboriki B, et al. Infection frequency of hepatitis C virus and IL28B haplotypes in Papua New Guinea, Fiji, and Kiribati. PLoS One. 2013;8(8):e66749.

109. Ministry of Health Republic of Indonesia. [Report on the National Basic Health Research (RISKESDAS) 2007]. Jakarta; 2010.

110. Registry FID. Finnish Infectious Disease Registry Statistical Database 2014 [Available from: http://www.thl.fi/ttr/gen/rpt/tilastot.html.

111. Dalgard O, Jeansson S, Skaug K, Raknerud N, Bell H. Hepatitis C in the general adult population of Oslo: prevalence and clinical spectrum. Scand J Gastroenterol. 2003;38(8):864-70.

112. Meffre C, Le Strat Y, Delarocque-Astagneau E, Dubois F, Antona D, Lemasson JM, et al. Prevalence of hepatitis B and hepatitis C virus infections in France in 2004: social factors are important predictors after adjusting for known risk factors. J Med Virol. 2010;82(4):546-55.

113. INVS. [National reference lab data for hepatitis C, 2001-2007] Surveillance nationale de l'hépatite C à partir des pôles de référence, données épidémiologiques 2001-2007 Saint-Maurice

cedex, France: Institut de Veille Sanitaire; 2009 [updated 2009. Available from: http://www.invs.sante.fr/content/download/6760/44658/version/1/file/web-2007v2.pdf.

114. Njouom R, Caron M, Besson G, Ndong-Atome GR, Makuwa M, Pouillot R, et al. Phylogeography, risk factors and genetic history of hepatitis C virus in Gabon, central Africa. PLoS One. 2012;7(8):e42002.

115. Ndong-Atome GR, Makuwa M, Ouwe-Missi-Oukem-Boyer O, Pybus OG, Branger M, Le Hello S, et al. High prevalence of hepatitis C virus infection and predominance of genotype 4 in rural Gabon. J Med Virol. 2008;80(9):1581-7.

116. Peto TJ, Mendy ME, Lowe Y, Webb EL, Whittle HC, Hall AJ. Efficacy and effectiveness of infant vaccination against chronic hepatitis B in the Gambia Hepatitis Intervention Study (1986-90) and in the nationwide immunisation program. BMC Infectious Diseases. 2014;14(1).

117. Health NCfDCP. National Population Survey 2015. 2015.

118. Butsashvili M, Tsertsvadze T, McNutt LA, Kamkamidze G, Gvetadze R, Badridze N. Prevalence of hepatitis B, hepatitis C, syphilis and HIV in Georgian blood donors. EurJEpidemiol. 2001;17(7):693-5.

119. Poethko-Muller C, Zimmermann R, Hamouda O, Faber M, Stark K, Ross RS, et al. [Epidemiology of hepatitis A, B, and C among adults in Germany: results of the German Health Interview and Examination Survey for Adults (DEGS1)]. Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz. 2013;56(5-6):707-15.

120. Hourfar MK, Jork C, Schottstedt V, Weber-Schehl M, Brixner V, Busch MP, et al. Experience of German Red Cross blood donor services with nucleic acid testing: results of screening more than 30 million blood donations for human immunodeficiency virus-1, hepatitis C virus, and hepatitis B virus. Transfusion. 2008;48(8):1558-66.

121. Institute RK. SurvStat 2013 [updated 2013. Available from: http://www3.rki.de/SurvStat.

122. Papatheodoridis G, Sypsa V, Kantzanou M, Nikolakopoulos I, Hatzakis A. Estimating the treatment cascade of chronic hepatitis B and C in Greece using a telephone survey. J Viral Hepat. 2015;22(4):409-15.

123. Gogos CA, Fouka KP, Nikiforidis G, Avgeridis K, Sakellaropoulos G, Bassaris H, et al. Prevalence of hepatitis B and C virus infection in the general population and selected groups in South-Western Greece. EurJEpidemiol. 2003;18(6):551-7.

124. Katsoulidou A, Moschidis Z, Sypsa V, Chini M, Papatheodoridis GV, Tassopoulos NC, et al. Analytical and clinical sensitivity of the Procleix Ultrio HIV-1/HCV/HBV assay in samples with a low viral load. Vox Sang. 2007;92(1):8-14.

125. Sypsa V, Touloumi G, Tassopoulos NC, Ketikoglou I, Vafiadis I, Hatzis G, et al. Reconstructing and predicting the hepatitis C virus epidemic in Greece: increasing trends of cirrhosis and hepatocellular carcinoma despite the decline in incidence of HCV infection. J Viral Hepat. 2004;11(4):366-74.

126. Gelu-Simeon M, Pillas V, Deloumeaux J, Delacroix-Maillard H, Saint-Georges G, Do Amaral L, et al. Seroepidemiology of chronic hepatitis B and C in the French Caribbean Island of Guadeloupe. BMC Research Notes. 2014;7:55-.

127. UNAIDS. High Coverage Sites: HIV prevention among injection drug users in transitional and developing countries. In: Collection UBP, editor. 2006.

128. Wong VW, Wong GL, Chim AM, Cheng TF, Cheung SW, Lai CM, et al. Targeted hepatitis C screening among ex-injection drug users in the community. J Gastroenterol Hepatol. 2014;29(1):116-20.

129. Department of Health. Surveillance of Viral Hepatitis in Hong Kong – 2014 Update Report. 2015.

130. Seto WK, Lai CL, Fung J, Hung I, Yuen J, Young J, et al. Natural history of chronic hepatitis C: Genotype 1 versus genotype 6. Journal of Hepatology. 2010;53(3):444-8.

131. Muller Z, Deak J, Horanyi M, Szekeres, Nagy I, Ozsvar Z, et al. The detection of hepatitis C virus in South Hungary. Journal of Clinical Virology. 2001;20(1-2):81-3.

132. Gillespie T. Prevalence, genotype distribution and outcome of hepatitis C infections among the employees of the Hungarian Central Hospital for Infectious diseases. Journal of Hospital Infection. 2001;49(4):239-44.

133. Puri P, Anand AC, Saraswat VA, Acharya SK, Sarin SK, Dhiman RK, et al. Consensus statement of HCV task force of the Indian National Association for Study of the Liver (INASL). Part II: INASL recommendations for management of HCV in India. Journal of Clinical and Experimental Hepatology. 2014;4(2):117-40.

134. Bagga PK, Singh SP. Seroprevalence of hepatitis C antibodies in healthy blood donors--a prospective study. Indian J Pathol Microbiol. 2007;50(2):429-32.

135. Chowdhury A, Santra A, Chaudhuri S, Dhali GK, Chaudhuri S, Maity SG, et al. Hepatitis C virus infection in the general population: a community-based study in West Bengal, India. Hepatology. 2003;37(4):802-9.

136. Inoue G, Horiike N, Michitaka K, Onji M. Hepatitis C virus clearance is prominent in women in an endemic area. J Gastroenterol Hepatol. 2000;15(9):1054-8.

137. Merat S, Rezvan H, Nouraie M, Jafari E, Abolghasemi H, Radmard AR, et al. Seroprevalence of hepatitis C virus: the first population-based study from Iran. Int J Infect Dis. 2010;14 Suppl 3:e113-6.

138. Shakeri MT, Nomani H, Ghayour MM, Sima HR, Gerayli S, Shahbazi S, et al. The prevalence of hepatitis C virus in mashhad, iran: a population-based study. Hepat Mon. 2013;13(3):e7723.

139. Zamani F, Sohrabi M, Poustchi H, Keyvani H, Saeedian FS, Ajdarkosh H, et al. Prevalence and risk factors of hepatitis C virus infection in amol city, north of iran: a population-based study (2008-2011). Hepat Mon. 2013;13(12):e13313.

140. Jamali R, Khonsari M, Merat S, Khoshnia M, Jafari E, Bahram KA, et al. Persistent alanine aminotransferase elevation among the general Iranian population: prevalence and causes. World JGastroenterol. 2008;14(18):2867-71.

141. Poustchi H, Esmaili S, Mohamadkhani A, Nikmahzar A, Pourshams A, Sepanlou SG, et al. The impact of illicit drug use on spontaneous hepatitis C clearance: experience from a large cohort population study. PLoS One. 2011;6(8):e23830.

142. Tarky AM, Akram W, Al-Naaimi AS, Omer AR. Epidemiology of viral hepatitis B and C in Iraq: a national survey 2005-2006. Zanco Journal of Medical Sciences. 2013;17(1):370-80.

143. Al-Kubaisy W. Specific HCV antibodies, RNA, and genotypes detection correlated to the age of pregnant women in Iraq. International Journal of Infectious Diseases. 2012;16:e67.

144. Thornton L, Murphy N, Jones L, Connell J, Dooley S, Gavin S, et al. Determination of the burden of hepatitis C virus infection in Ireland. Epidemiol Infect. 2012;140(8):1461-8.

145. Health Protection Surveillance C. Epidemiology of Hepatitis C in Ireland, 2012. 2013.

146. Cornberg M, Razavi HA, Alberti A, Bernasconi E, Buti M, Cooper C, et al. A systematic review of hepatitis C virus epidemiology in Europe, Canada and Israel. Liver International. 2011;31(SUPPL. 2):30-60.

147. Sermoneta-Gertel S, Donchin M, Adler R, Baras M, Perlstein T, Manny N, et al. Hepatitis c virus infection in employees of a large university hospital in Israel. Infect Control Hosp Epidemiol. 2001;22(12):754-61.

148. Ansaldi F, Bruzzone B, Salmaso S, Rota MC, Durando P, Gasparini R, et al. Different seroprevalence and molecular epidemiology patterns of hepatitis C virus infection in Italy. J Med Virol. 2005;76(3):327-32.

149. Marcellusi A, Viti R, Capone A, Mennini FS. Direct and Indirect Cost of HCV-Related Diseases in Italy: An Incidence-Based Probabilistic Approach. Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research. 2014;17(7):A671.

150. Cozzolongo R, Osella AR, Elba S, Petruzzi J, Buongiorno G, Giannuzzi V, et al. Epidemiology of HCV infection in the general population: a survey in a southern Italian town. AmJGastroenterol. 2009;104(11):2740-6.

151. Fusco M, Girardi E, Piselli P, Palombino R, Polesel J, Maione C, et al. Epidemiology of viral hepatitis infections in an area of southern Italy with high incidence rates of liver cancer. European Journal of Cancer. 2008;44(6):847-53.

152. Tanaka J, Katayama K. [Hepatitis C virus infection in japan--epidemiology]. Nihon rinsho Japanese journal of clinical medicine. 2011;69 Suppl 4:15-22.

153. Al Abaddi B, Al Amr M, Abasi L, Saleem A, Abu Hazeem N, Marafi A. Seroprevalence of HBV, HCV, HIV and syphilis infections among blood donors at Blood Bank of King Hussein Medical Center: a 3 year study. Middle East Journal of Family Medicine. 2014;12(6):10-3.

154. Jbara I, Abu Alshiekh NK, Almomani AM, Khasawneh RH, Omari AK. Prevalence of hepatitis C virus antibodies among blood donors at Prince Hashem Hospital, Zarka-Jordan. Jordan Medical Journal. 2006;40(3):190-3.

155. Abou Rached A, Abou Kheir S, Saba J, Ammar W. Epidemiology of hepatitis B and hepatitis C in Lebanon. Arab Journal of Gastroenterology. 2016;17(1):29-33.

156. MA X, BC Z, LY G. Overview of the epidemiological situation of HIV - infection and sentinel surveillance (SS) in the Republic of Kazakhstan for 2007. Almaty, Kazakhstan; 2009 2009.

157. Iashina TL, Favorov MO, Shakhgil'dian IV, Iarasheva DM, Nazarova OI, Derevianko EN, et al. [The spread of hepatitis C markers among the population of regions of Russia and Central Asia]. Zh Mikrobiol Epidemiol Immunobiol. 1993(5):46-9.

158. Kerubo G, Khamadi S, Okoth V, Madise N, Ezeh A, Abdalla Z, et al. Hepatitis B, Hepatitis C and HIV-1 Coinfection in Two Informal Urban Settlements in Nairobi, Kenya. PLoS One. 2015;10(6):e0129247.

159. Abdalla F, Mwanda OW, Rana F. Comparing walk-in and call-responsive donors in a national and a private hospital in Nairobi. East Afr Med J. 2005;82(10):531-5.

160. KASL clinical practice guidelines: management of hepatitis C. Clin Mol Hepatol. 2014;20(2):89-136.

161. Kim dY, Kim IH, Jeong SH, Cho YK, Lee JH, Jin YJ, et al. A nationwide seroepidemiology of hepatitis C virus infection in South Korea. Liver Int. 2013;33(4):586-94.

162. Tolmane I, Rozentale B, Keiss J, Arsa F, Brigis G, Zvaigzne A. The prevalence of viral hepatitis C in Latvia: a population-based study. Medicina (Kaunas). 2011;47(10):532-5.

163. Centre for Disease P, Control of L. [Reports on infectious and parasitic diseases in 2010-2014]. Riga, Latvia: Centre for Disease Prevention and Control of Latvia; 2015.

164. Araj GF, Kfoury-Baz EE, Barada KA, Nassif RE, Alami SY. Hepatitis C virus : prevalence in Lebanese blood donors and brief overview of the disease. Le Journal m+¬dical libanais The Lebanese medical journal. 1995;43(1):11-6.

165. Baddoura R, Haddad C, Germanos M. Hepatitis B and C seroprevalence in the Lebanese population. East MediterrHealth J. 2002;8(1):150-6.

166. Abou-Rached. Lebanon HCV prevalence study on general population. Unknown. 2015.

167. Alashek W, Altagdi M. Risk factors and genotypes of hepatitis C virus infection in libyan patients. Libyan J Med. 2008;3(4):162-5.

168. Liakina V, Valantinas J. Anti-HCV prevalence in the general population of Lithuania. Med Sci Monit. 2012;18(3):Ph28-35.

169. Mossong J, . Hepatitis C in Luxembourg: a preliminary epideiological analysis of cases confirmed at the National Health Laboratory, 1990-2013. 2014.

170. Devaux C. Report HCV CHL database Luxembourg. 2014.

171. Ramarokoto CE, Rakotomanana F, Ratsitorahina M, Raharimanga V, Razafindratsimandresy R, Randremanana R, et al. Seroprevalence of hepatitis C and associated risk factors in urban areas of Antananarivo, Madagascar. BMC Infect Dis. 2008;8:25.

172. Razafindratsimandresy R, Dubot A, Ramarokoto CE, Iehle C, Soares JL, Rousset D. Hepatitis C virus infection and genotypes in Antananarivo, Madagascar. J Med Virol. 2007;79(8):1082-8.

173. McDonald SA, Mohamed R, Dahlui M, Naning H, Kamarulzaman A. Bridging the data gaps in the epidemiology of hepatitis C virus infection in Malaysia using multi-parameter evidence synthesis. BMC Infectious Diseases. 2014:564.

174. Lee WS, Ng KP. Seroprevalence of anti-HCV in an urban child population: a preliminary study from Kuala Lumpur. Singapore Med J. 2001;42(3):100-1.

175. MA Z. Management of hepatitis C: Malaysian Society of Gastroenterology and Hepatology; 2013 [updated 2013. Available from: http://www.msgh.org.my/resources/managementhepatitisc.htm.

176. Haslina MN, Khairiah Y, Zainy DZ, Shafini MY, Rosnah B, Marini R. Seroprevalence of hepatitis C virus infection among blood donors in a teaching hospital in northeastern Malaysia. Southeast Asian J Trop Med Public Health. 2012;43(3):668-73.

177. McDonald SA, Hutchinson SJ, Schnier C, McLeod A, Goldberg DJ. Estimating the number of injecting drug users in Scotland's HCV-diagnosed population using capture-recapture methods. Epidemiology and Infection. 2014;142(1):200-7.

178. Brincat A, Azzopardi N, Deguara M, Taliana KM, Rogers M, Pocock J. The management of patients positive to Hepatitis C antibody in Malta. Malta Medical Journal. 2013;25(4):72-7.

179. Valdespino JL, Conde-González CJ, Olaiz-Fernández G, Palma O, Kershenobich D, Sepúlveda J. Seroprevalence of hepatitis C among Mexican adults: an emerging public health problem? Salud pública Méx. 2007;49:s395-s403.

180. Tserenpuntsag B, Tserenpuntsag B, Kuydowicz J, Jablonowska E. [Primary hepatotropic viral infections in Mongolia]. Przegl Epidemiol. 2008;62(2):425-32.

181. Baatarkhuu O, Kim do Y, Ahn SH, Nymadawa P, Dahgwahdorj Y, Shagdarsuren M, et al. Prevalence and genotype distribution of hepatitis C virus among apparently healthy individuals in Mongolia: a population-based nationwide study. Liver Int. 2008;28(10):1389-95.

182. Khoudri I, editor Moroccan experience to ensure access to prevention and treatment of hepatitis. Strategic and technical consultation on viral hepatitis in the Eastern Mediterranean Region; 2016 April 25-27, 2016; Casablanca, Morocco.

183. Belbacha I, Cherkaoui I, Akrim M, Dooley KE, El Aouad R. Seroprevalence of hepatitis B and C among barbers and their clients in the Rabat region of Morocco. East Mediterr Health J. 2011;17(12):911-9.

184. Benouda A, Boujdiya Z, Ahid S, Abouqal R, Adnaoui M. [Prevalence of hepatitis C virus infection in Morocco and serological tests assessment of detection for the viremia prediction]. Pathol Biol (Paris). 2009;57(5):368-72.

185. Baha W, Foullous A, Dersi N, They-they TP, El aK, Nourichafi N, et al. Prevalence and risk factors of hepatitis B and C virus infections among the general population and blood donors in Morocco. BMC Public Health. 2013;13:50.

186. Vriend HJ, Van Veen MG, Prins M, Urbanus AT, Boot HJ, Op De Coul EL. Hepatitis C virus prevalence in The Netherlands: migrants account for most infections. Epidemiol Infect. 2013;141(6):1310-7.

187. Micallef JM, Kaldor JM, Dore GJ. Spontaneous viral clearance following acute hepatitis C infection: A systematic review of longitudinal studies. J Viral Hepat. 2006;13(1):34-41.

188. The Hepatitis Foundation of New Z. Hepatitis C2013.

189. Nesdale A, Baker M, Gane E, Kemp R, Brunton C, Law M, et al. Hepatitis C infection in New Zealand: Estimating the current and future prevalence and impact. 2000 7/1/2000.

190. Okwuraiwe A, Salu OB, Anomneze EE, Audu R, Ujah A. Hepatitis C Virus Genotypes and Viral Ribonucleic Acid Titers in Nigeria. Nigerian Journal of Gastroenterology and Hepatology. 2012;4(2):67-72.

191. Schuster H, Serebour E, Nograles J, Al-Belushi I, Hassan K. Prevelance of blood-borne viruses amongst antenatal clinic patients and blood donors in a tertiary referral hospital in Oman. Clinical Microbiology and Infection. 2009;15:S587.

192. Al Naamani K. Epidemiology of HCV in Oman. 2015.

193. Khan NU, Ali I, Ahmad NU, Iqbal A, Rehman LU, Munir I, et al. Prevalence of active HCV infection among the blood donors of Khyber Pakhtunkwa and FATA region of Pakistan and evaluation of the screening tests for anti-HCV. Virol J. 2011;8:154.

194. Fukuda Y, Inaoka T, Futatsuka M, Kawabata M, Ataka Y, Ohtsuka R. Serological survey for viral infections in Austronesian-speaking Balopa Islanders, Papua New Guinea. Kumamoto Medical Journal. 1999;46(2):47-54.

195. Alejandro CY, Rolando FB, Armando M, Eduardo Z, Jorge F, Alejandro B, et al. Prevalencia serológica de anticuerpos al virus de la Hepatitis C en personal de salud en el Perú. Revista de Gastroenterología del Perú. 2004:13-20.

196. Yanase Y, Ohida T, Kaneita Y, Agdamag DM, Leano PS, Gill CJ. The prevalence of HIV, HBV and HCV among Filipino blood donors and overseas work visa applicants. BullWorld Health Organ. 2007;85(2):131-7.

197. Agdamag DM, Kageyama S, Alesna ET, Solante RM, Leano PS, Heredia AM, et al. Rapid spread of hepatitis C virus among injecting-drug users in the Philippines: Implications for HIV epidemics. J Med Virol. 2005;77(2):221-6.

198. Katayama Y, Barzaga NG, Alipio A, Soetjipto, Doi H, Ishido S, et al. Genotype analysis of hepatitis C virus among blood donors and inmates in Metro Manila, The Philippines. Microbiol Immunol. 1996;40(7):525-9.

199. Godzik P, Kolakowska A, Madalinski K, Stepien M, Zielinski A, Goralewska A, et al. [Prevalence of anti-HCV antibodies among adults in Poland--results of cross-sectional study in general population]. Przegl Epidemiol. 2012;66(4):575-80.

200. (NIPH-NIH) NIoPH-NIoH. [Infectious diseases and poisonings in Poland in 2012]. Warsaw, Poland; 2013 2013.

201. Marinho RT, Moura MC, Giria JA, Ferrinho P. Epidemiological aspects of hepatitis C in Portugal. J Gastroenterol Hepatol. 2001;16(9):1076-7.

202. Peixe P. The epidemiological situation of hepatitis C in Portugal 2010 [updated 2010. Available from: http://www.vhpb.org/files/html/Meetings_and_publications/Presentations/LISS33.pdf.

203. Dubois F, Desenclos JC, Mariotte N, Goudeau A. Hepatitis C in a French population-based survey, 1994: Seroprevalence, frequency of viremia, genotype distribution, and risk factors. The Collaborative Study Group. Hepatology. 1997;25(6):1490-6.

204. Sola R, Cruz De Castro E, Hombrados M, Planas R, Coll S, Jardi R, et al. [Prevalence of hepatitis B and hepatitis C viruses in different counties of Catalonia, Spain: cross-sectional study]. Med Clin (Barc). 2002;119(3):90-5.

205. Guadagnino V, Zimatore G, Rocca A, Montesano F, Masciari R, Caroleo B, et al. Anti-hepatitis C antibody prevalence among intravenous drug addicts in the Catanzaro area. Arch Virol Suppl. 1992;4:335-6.

206. Perez CM, Marrero E, Melendez M, Adrovet S, Colon H, Albizu C, et al. Feasibility of collecting biologic specimens in population-based surveys: experiences from the epidemiology of hepatitis C in the household, adult population of Puerto Rico study. P R Health Sci J. 2010;29(1):18-25.

207. Sharma K. Unpublished data on HCV age and gender distribution from a national study in Qatar. 2015.

208. Gheorghe L, Csiki IE, Iacob S, Gheorghe C, Smira G, Regep L. The prevalence and risk factors of hepatitis C virus infection in adult population in Romania: a nationwide survey 2006 - 2008. J Gastrointestin Liver Dis. 2010;19(4):373-9.

209. Zhiburt EB, Asadi AK, Cherkasov EG, Reizman PV. [The verification of the results of screening antibodies to hepatitis C virus in blood donors]. Zh Mikrobiol Epidemiol Immunobiol. 2005(5):71-3.

210. Shustov AV, Kochneva GV, Sivolobova GF, Grazhdantseva AA, Gavrilova IV, Akinfeeva LA, et al. Molecular epidemiology of the hepatitis C virus in Western Siberia. J Med Virol. 2005;77(3):382-9.

211. Armstrong GL, Williams IT, Maga UA, Viali S, Kuhnert WL, McGarvey ST. Hepatitis C virus infection in Samoa and American Samoa. Am J Trop Med Hyg. 2006;74(2):261-2.

212. Bashawri LA, Fawaz NA, Ahmad MS, Qadi AA, Almawi WY. Prevalence of seromarkers of HBV and HCV among blood donors in eastern Saudi Arabia, 1998-2001. Clin Lab Haematol. 2004;26(3):225-8.

213. Sievert W, Altraif I, Razavi HA, Abdo A, Ahmed EA, Alomair A, et al. A systematic review of hepatitis C virus epidemiology in Asia, Australia and Egypt. Liver Int. 2011;31 Suppl 2:61-80.

214. WHO. The growing threats of hepatitis B and C in the Eastern Mediterranean Region; A call for action. World Health Organization Regional Committee for the Eastern Mediterranean Web: World Health Organization; 2009 [

215. Schreter I, Kristian P, Klement C, Kohutova D, Jarcuska P, Madarova L, et al. [Prevalence of hepatitis C virus infection in Slovakia]. Klin Mikrobiol Infekc Lek. 2007;13(2):54-8.

216. P K, I S. Hepatitis C virus (HCV) prevalence in Slovakia. In: Razavi H, E G, editors. 2014.

217. Sibley A, Han KH, Abourached A, Lesmana LA, Makara M, Jafari W, et al. The present and future disease burden of hepatitis C virus (HCV) infections with today's treatment paradigm - volume 3. J Viral Hepat. 2015.

218. Seme K, Vrhovac M, Mocilnik T, Maticic M, Lesnicar G, Baklan Z, et al. Hepatitis C virus genotypes in 1,504 patients in Slovenia, 1993-2007. J Med Virol. 2009;81(4):634-9.

219. Parboosing R, Paruk I, Lalloo UG. Hepatitis C virus seropositivity in a South African Cohort of HIV co-infected, ARV naive patients is associated with renal insufficiency and increased mortality. J Med Virol. 2008;80(9):1530-6.

220. Prabdial-Sing N, Puren AJ, Mahlangu J, Barrow P, Bowyer SM. Hepatitis C virus genotypes in two different patient cohorts in Johannesburg, South Africa. Arch Virol. 2008;153(11):2049-58.

221. Denniston MM, Jiles RB, Drobeniuc J, Klevens RM, Ward JW, McQuillan GM, et al. Chronic hepatitis C virus infection in the United States, National Health and Nutrition Examination Survey 2003 to 2010. Ann Intern Med. 2014;160(5):293-300.

222. Gutierrez-Zufiaurre N, Sanchez-Hernandez J, Munoz S, Marin R, Delgado N, Saenz MC, et al. [Seroprevalence of antibodies against Treponema pallidum, Toxoplasma gondii, rubella virus, hepatitis B and C virus, and HIV in pregnant women]. EnfermInfeccMicrobiolClin. 2004;22(9):512-6.

223. Generalitat de Catalunya Department de S. [Activities Report: Year 2010. Advisory Council on Drug Treatment of Viral Hepatitis]. Barcelona, Spain: Generalitat de Catalunya Dpeartment de Salut; 2011.

224. Duberg AS, Blach S, Falconer K, Kaberg M, Razavi H, Aleman S. The future disease burden of hepatitis C virus infection in Sweden and the impact of different treatment strategies. Scand J Gastroenterol. 2014:1-12.

225. Duberg A, Janzon R, Back E, Ekdahl K, Blaxhult A. The epidemiology of hepatitis C virus infection in Sweden. Euro Surveill. 2008;13(21).

226. Ydreborg M, Soderstrom A, Hakanson A, Alsio A, Arnholm B, Malmstrom P, et al. Look-back screening for the identification of transfusion-induced hepatitis C virus infection in Sweden. Scand J Infect Dis. 2011;43(6-7):522-7.

227. Lidman C, Norden L, Kaberg M, Kall K, Franck J, Aleman S, et al. Hepatitis C infection among injection drug users in Stockholm Sweden: prevalence and gender. Scand J Infect Dis. 2009;41(9):679-84.

228. Sagmeister M, Renner EL, Mullhaupt B, Wong JB. Simulation of hepatitis C based on a mandatory reporting system. Eur J Gastroenterol Hepatol. 2002;14(1):25-34.

229. Fretz R, Negro F, Bruggmann P, Lavanchy D, De Gottardi A, Pache I, et al. Hepatitis B and C in Switzerland - healthcare provider initiated testing for chronic hepatitis B and C infection. Swiss Med Wkly. 2013;143:w13793.

230. Health SFOoP. Number of hepatitis C cases reported in Switzerland between 1988 and 2012 by year of birth (mandatory notification of laboratory confirmed cases): FOPH/ID/EPI/RIC. 2013 2013.

231. Karim M, Lanham H. Prevalence of viral hepatitis B and C in Syria. Syrian Epidemiological Bulletin, World Health Organization. 2008;2(3):2.

232. Abdulkarim AS, Zein NN, Germer JJ, Kolbert CP, Kabbani L, Krajnik KL, et al. Hepatitis C virus genotypes and hepatitis G virus in hemodialysis patients from Syria: identification of two novel hepatitis C virus subtypes. Am J Trop Med Hyg. 1998;59(4):571-6.

233. Yu ML, Yeh ML, Tsai PC, Huang CI, Huang JF, Huang CF, et al. Huge gap between clinical efficacy and community effectiveness in the treatment of chronic hepatitis C: a nationwide survey in Taiwan. Medicine (Baltimore). 2015;94(13):e690.

234. Chen CH, Yang PM, Huang GT, Lee HS, Sung JL, Sheu JC. Estimation of seroprevalence of hepatitis B virus and hepatitis C virus in Taiwan from a large-scale survey of free hepatitis screening participants. JFormosMedAssoc. 2007;106(2):148-55.

235. Yang C, Latkin C, Luan R, Wang C, Nelson K. HIV, syphilis, hepatitis C and risk behaviours among commercial sex male clients in Sichuan province, China. Sex Transm Infect. 2010;86(7):559-64.

236. Wasitthankasem R PN, Vichaiwattana P, et al. . Decreasing Hepatitis C Virus Infection in Thailand in the Past Decade: Evidence from the 2014 National Survey. PLoS ONE. 2016;11(2).

237. Sunanchaikarn S, Theamboonlers A, Chongsrisawat V, Yoocharoen P, Tharmaphornpilas P, Warinsathien P, et al. Seroepidemiology and genotypes of hepatitis C virus in Thailand. Asian Pacific Journal of Allergy and Immunology. 2007;25(2-3):175-82.

238. Mejri S, Salah AB, Triki H, Alaya NB, Djebbi A, Dellagi K. Contrasting patterns of hepatitis C virus infection in two regions from Tunisia. J Med Virol. 2005;76(2):185-93.

239. Tozun N, Ozdogan OC, Cakaloglu Y, Idilman R, Karasu Z, Akarca US, et al. A nationwide prevalence study and risk factors for hepatitis A, B, C and D infections in Turkey. Hepatology. 2010;52:697A.

240. Dursun M, Ozekinci T, Ertem M, Saka G, Yilmaz S, Canoruc F, et al. Prevalence of Hepatitis C in adults in the south-eastern region of Anatolia: a community-based study. Hepatol Res. 2004;29(2):75-80.

241. Yildirim B, Barut S, Bulut Y, Yenisehirli G, Ozdemir M, Cetin I, et al. Seroprevalence of hepatitis B and C viruses in the province of Tokat in the Black Sea region of Turkey: A population-based study. TurkJ Gastroenterol. 2009;20(1):27-30.

242. Al Shaer L, Abdul Rahman M, John TJ, Al Hashimi A. Trends in prevalence, incidence, and residual risk of major transfusion-transmissible viral infections in United Arab Emirates blood donors: Impact of individual-donation nucleic acid testing, 2004 through 2009. Transfusion. 2012;52(11):2300-9.

243. Harris RJ, Ramsay M, Hope VD, Brant L, Hickman M, Foster GR, et al. Hepatitis C prevalence in England remains low and varies by ethnicity: An updated evidence synthesis. Eur J Public Health. 2012;22(2):187-92.

244. Hutchinson SJ, Roy KM, Wadd S, Bird SM, Taylor A, Anderson E, et al. Hepatitis C virus infection in Scotland: epidemiological review and public health challenges. Scott Med J. 2006;51(2):8-15.

245. Collins S, Lattimore S. Sentinel surveillance of hepatitis testing in England-hepatitis C testing 2010 report analyses of HCV testing data between 2007 and 2010: Health Protection Agency; 2011 [updated 2011. Available from: http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1313155286634.

246. Edlin BR, Eckhardt BJ, Shu MA, Holmberg SD, Swan T. Toward a more accurate estimate of the prevalence of hepatitis C in the United States. Hepatology. 2015;62(5):1353-63.

247. Chak E, Talal A, Sherman KE, Schiff E, Saab S. Hepatitis C virus infection in the United States: an estimate of true prevalence. Liver Int. 2011;31(8):1090-101.

248. Centers for Disease C, Prevention. National Center for Health S. National Health and Nutrition Examination Survey Data, 2003-2014. Hyattsville, MD: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention.; 2015.

249. Aguilar MS, Cosson C, Loureiro CL, Devesa M, Martinez J, Villegas L, et al. Prevalence of infection with hepatitis C virus in Venezuela, as assessed with an immuno-assay based on synthetic peptides. Ann Trop Med Parasitol. 2001;95(2):187-95.

250. César C-S, Reyna M-P, Evelyn C-V, Raimy M-M, Mary A-S, Diana C-M, et al. Seroprevalencia del Virus de Hepatitis C (VHC) en pacientes del Laboratorio Regional de Referencia Virológica (Maracaibo, Venezuela). Revista de Gastroenterología del Perú. 2005:248-53.

251. Cuadra-Sanchez C, Moronta-Pinango R, Cordova-Villanueva E, Mindiola-Morles R, Araujo Soto M, Callejas-Monsalve D, et al. [Seroprevalence of Hepatitis C Virus (HCV) in patients of the Regional Viral Reference Laboratory (Maracaibo, Venezuela)]. Rev Gastroenterol Peru. 2005;25(3):248-53.

252. Do SH, Yamada H, Fujimoto M, Ohisa M, Matsuo J, Akita T, et al. High prevalences of hepatitis B and C virus infections among adults living in Binh Thuan province, Vietnam. Hepatology Research. 2015;45(3):259-68.

253. Gacche RN, Al-Mohani SK. Seroprevalence and Risk Factors for Hepatitis C Virus Infection among General Population in Central Region of Yemen. Hepat Res Treat. 2012;2012:689726.

254. Al-Nabehi BAH, Al-Shamahy H, Saeed WSE, Musa AM, El Hassan AM, Khalil EAG. Sero-molecular epidemiology and risk factors of viral hepatitis in urban Yemen. International Journal of Virology. 2015;11(3):133-8.

255. Division UNDoEaSAP. World population prospects: The 2012 revision New York: United Nations; 2014 [updated 2014 Online version updates various data. Available from: http://esa.un.org/unpd/wpp/index.htm.

256. IRODaT. International Registry on Organ Donation and Transplantation Barcelona, Spain: IRODaT; 2015 [updated 7/26/2015. Available from: http://www.irodat.org/?p=database&c=HU&year=2013#data.

257. Harris RJ, Thomas B, Griffiths J, Costella A, Chapman R, Ramsay M, et al. Increased uptake and new therapies are needed to avert rising hepatitis C-related end stage liver disease in England: modelling the predicted impact of treatment under different scenarios. J Hepatol. 2014;61(3):530-7.

258. Bernfort L, Sennfalt K, Reichard O. Cost-effectiveness of peginterferon alfa-2b in combination with ribavirin as initial treatment for chronic hepatitis C in Sweden. Scand J Infect Dis. 2006;38(6-7):497-505.

259. Ries L, Young G, Keel G, Eisner M, Lin Y, Horner M. SEER survival monograph: Cancer survival among adults: U.S. SEER program, 1988-2001, patient and tumor characteristics. Bethesda, MD: National Cancer Institute, SEER Program; 2007.

260. Guerra J, Garenne M, Mohamed MK, Fontanet A. HCV burden of infection in Egypt: results from a nationwide survey. J Viral Hepat. 2012;19(8):560-7.

261. El-Zanaty F, Way A. Egypt demographic and health survey, 2008. Cairo: Cairo, Egypt : Ministry of Health and Population, 2009; 2009. p. 431.

262. McQuillan G, D K-M, MM D, R H. Viral hepatitis. Hyattsville, MD; 2010 3/2010.

Appendices

Appendix 1: Input data for prevalence of HCV infection, by age, and proportion of viraemic among persons with serological evidence of past or current HCV infection, and sources of information

Country	Prev. Est. Status	Anti-HCV Prevalence - Base	Study Year	Data Quality Score	Anti-HCV Prevalence - Low	Anti-HCV Prevalence- High	Percent Viraemic	Source (base)	Source (low)	Source (high)	Age source	Percent Viraemic Source Type	Percent Viraemic Source
Afghanistan	E	1.10%	2003-2011	2	0.40%	1.92%	57.50%	(44)	(45)	(46)	EX (37)	PS	(47)
Algeria	E	1.40%	2011*	1	0.24%	2.50%	75.20%	(48)	(48)	(48)	EX (49)	PS	(48)
Argentina	A	1.50%	2007	1	0.32%	2.00%	80.00%	(29)	(50)	(51)	(29, 52)	PS	(53)
Australia	A	1.30%	2012	2	1.20%	1.85%	74.65%	(54)	(55)	(55)	(56)	NS	(57)
Austria	A	0.50%	2008	1	0.10%	0.70%	73.88%	(55, 58)	(58)	(59)	EC (55)	PS	(58)
Azerbaijan	E	3.70%	2010	2	--	--	71.00%	(60)	E	E	EX (61)	EX	(62)
Bahrain	A	1.70%	2011	1	1.00%	1.90%	77.00%	(63)	(63)	E	EC	PS	(64)
Belgium	A	0.87%	1994	1	0.12%	1.10%	80.00%	(24, 25)	(27)	(25, 28)	(65)	PS	(66)
Brazil	A	1.38%	2005-2009	3	1.12%	1.64%	80.50%	(67)	(67)	(67)	(68)	PS	(69)
Bulgaria	E	1.50%	2012	1	0.70%	2.43%	87.00%	(70, 71)	(72)	(71)	(73)	NS	(71)
Burkina Faso	E	3.50%**	2010	2	3.00%**	3.90%**	74.40%	(74)	(74)	(74)	(74)	EX	(75)
Burundi	E	8.20%	2002	3	--	11.0%	23.00%	(38)	E	(76)	(38)	EX	(77)
Cambodia	E	5.80%	2007-2009	2	2.30%	14.70%	39.30%	(17)	(78)	(79)	(17)	PS	(17)
Cameroon	A	1.03%	2011	1	0.80%	1.10%	75.00%	EC	EC (80)	EC (80)	EC	PS	(81)
Canada	A	0.96%	2011	2	0.61%	1.34%	77.00%	(82)	(82)	(82)	(83)	PS	(84)
Central African Republic	E	0.60%**	2010	3	--	1.73%**	61.00%	(85)	E	(86)	EX EC[1]	PS	(86)
Chad	E	2.00%**	2012	2	--	4.8%	65.40%	(87)	E	(88)	(87)	PS	(89)

Country	Prev. Est. Status	Anti-HCV Prevalence - Base	Study Year	Data Quality Score	Anti-HCV Prevalence - Low	Anti-HCV Prevalence- High	Percent Viraemic	Source (base)	Source (low)	Source (high)	Age source	Percent Viraemic Source Type	Percent Viraemic Source
Chile	E	0.83%	2000	2	0.35%	1.31%	62.50%	(90)	(90)	(90)	(90)	NS	(91)
China	E	1.21%	2015	2	0.93%	1.49%	60.00%	EC	(92)	(92)	(92)	PS	(93)
Colombia	E	1.31%	2011	1	0.83%	1.30%	80.00%	EC	(94)	(94)	(95)	EX	(53)
Croatia	A	0.90%	2010-2011	2	0.50%	1.40%	70.00%	(96)	(96)	(96)	EC	EC	EC
Cuba	E	0.60%	2003	2	0.19%	1.70%	76.10%	(97)	(97)	(97)	(98)	PS	(99)
Czech Republic	A	0.57%	2012	1	0.20%	0.70%	70.00%	(55)	(100)	(55)	EC	EC	(55)
Denmark	A	0.63%	2007	2	0.48%	0.72%	62.20%	(101)	(101)	(101)	(101)	PS	(101)
Dominican Republic	E	1.00%	2015	1	--	2.40%	65.20%	EC	E	(102)	(103)	EX	(104)
Egypt	A	10.00%	2014	3	7.10%	11.70%	69.84%	(33)	(33)	(33)	(33)	PS	(33)
Estonia	A	1.97%	2013	1	1.50%	2.00%	76.20%	(105)	(105)	(105)	(106)	EC	(105)
Ethiopia	A	0.96%	2000-2002	2	0.60%	1.20%	75.00%	(107)	(107)	(107)	(107)	EC	EC
Fiji	E	0.10%	2003 - 2005	1	0.01%	0.70%	69.00%	(108)	(108)	(108)	EX (109)	EX	(5)
Finland	A	0.50%	2012	1	0.60%	0.90%	79.50%	(29)	(29)	(29)	(110)	EX	(111)
France	A	0.84%	2004	3	0.45%	1.10%	65.00%	(112)	(112)	(112)	(112)	NS	(113)
Gabon	E	11.20%**	2005-2008	2	10.30%**	12.30%**	91.00%	(114)	(114)	(114)	(114)	PS	(115)
Gambia, The	E	0.50%	2002	2	0.50%	2.10%	74.40%	(116)	(116)	(116)	(116)	EX	(75)
Georgia	E	7.50%	2015	3	5.23%	6.26%	70.60%	(117)	E	(118)	(117)	PS	(117)
Germany	A	0.58%	2012	1	0.30%	0.90%	67.00%	(55)	(119)	(120)	(55, 119, 121)	PS	(119)
Ghana	A	2.10%	2014	2	1.20%	5.50%	74.40%	EC	EC	EC	EC	PS	(75)

Country	Prev. Est. Status	Anti-HCV Prevalence - Base	Study Year	Data Quality Score	Anti-HCV Prevalence - Low	Anti-HCV Prevalence- High	Percent Viraemic	Source (base)	Source (low)	Source (high)	Age source	Percent Viraemic Source Type	Percent Viraemic Source
Greece	A	1.79%	2011	3	0.50%	2.61%	80.00%	(122)	(123)	(122)	(124)	PS	(125)
Guadeloupe	E	0.55%	2006	2	0.28%	0.96%	71.40%	(126)	(126)	(126)	EX (103)	PS	(126)
Hong Kong Special Administrative Region	A	0.29%	2013	2	0.08%	0.50%	77.61%	EC (127-129)	(129)	(129)	(129)	PS	(130)
Hungary	A	0.70%	2014	1	0.40%	2.70%	75.00%	(105)	(131)	(132)	(105)	EC	EC
Iceland	A	0.41%	2013	2	0.33%	0.48%	80.00%	(105)	(105)	(105)	(105)	EC	EC
India	A	0.84%	2013	1	0.50%	1.50%	80.77%	(29)	(133)	(133)	(29, 134)	PS	(135)
Indonesia	A	0.80%	2007	3	0.10%	1.70%	65.70%	(109)	(109)	(109)	(109)	PS	(136)
Iran (Islamic Republic of)	A	0.50%	2006	2	0.20%	1.00%	62.00%	(137)	(138, 139)	(140)	(137)	PS	(141)
Iraq	E	0.40%	2000*	3	0.30%	0.50%	62.70%	(142)	(142)	(142)	(142)	PS	(143)
Ireland	A	0.70%	2010	2	0.67%	1.60%	75.00%	(144)	(144)	(144)	(145)	PS	(144)
Israel	A	1.96%	2001-2010	2	0.90%	2.10%	75.50%	(146)	(147)	(146)	(21, 29)	EC	(21, 29)
Italy	E	2.43%	2001	1	1.60%	7.30%	73.00%	(148, 149)	(148)	(148)	(148, 150)	PS	(151)
Japan	A	0.98%	2011	2	0.49%	2.20%	70.00%	(152)	(152)	(152)	(152)	PS	(152)
Jordan	A	0.42%	2011	2	0.10%	--	84.60%	(16)	(153)	E	(154)	EX	(155)
Kazakhstan	E	3.20%	2010	2	1.30%	--	71.00%	(20)	(156)	E	(20)	EX	(157)
Kenya	E	0.76%	2006 - 2007	2	0.20%	--	75.00%	(158)	(159)	E	(158)	EX	EC[2]
Korea, Republic of	A	1.20%	2013	1	0.80%	1.29%	56.10%	(105, 160)	(161)	(160)	(161)	PS	(161)
Latvia	A	2.40%	2008	2	1.70%	3.30%	71.40%	(162)	(162)	(162)	(163)	PS	(162)
Lebanon	A	0.21%	2011	2	0.11%	0.70%	84.60%	(155)	(164)	(165)	(155)	PS	(166)

Country	Prev. Est. Status	Anti-HCV Prevalence - Base	Study Year	Data Quality Score	Anti-HCV Prevalence - Low	Anti-HCV Prevalence- High	Percent Viraemic	Source (base)	Source (low)	Source (high)	Age source	Percent Viraemic Source Type	Percent Viraemic Source
Libya	E	1.20%	2004-2005	3	1.10%	1.30%	54.00%	(49)	(49)	(49)	(49)	PS	(167)
Lithuania	A	1.96%	2010	2	1.21%	2.71%	65.91%	(105, 168)	(105, 168)	(105, 168)	(105, 168)	EC	(105)
Luxembourg	A	1.34%	2006	1	0.56%	0.93%	77.00%	EC	EC	EC	(29, 169, 170)	EC	(29)
Madagascar	E	1.20%	2004	2	0.75%	1.72%	47.22%	(171, 172)	(171, 172)	(171, 172)	(171)	PS	(171, 172)
Malaysia	A	1.90%**	2011*	2	0.30%	7.70%	73.88%	(173, 174)	(175)	(176)	EC	PS	(177)
Malta	A	0.36%	2010	1	0.26%	0.60%	79.30%	(178)	(178)	(5)	(178)	PS	(178)
Mexico	A	1.40%	2000	3	1.10%	1.60%	65.20%	(179)	(179)	(179)	(179)	NS	(104)
Mongolia	A	9.80%	2010	3	8.70%	15.60%	70.00%	EC	(180)	(181)	(181)	EC	EC
Morocco	E	1.20%	2008	2	1.10%	1.93%	75.00%	(182)	(183)	(184)	EC (185)	EC	EC
Netherlands	A	0.22%	2009	2	0.07%	0.37%	74.00%	(186)	(186)	(186)	(29)	PS	(187)
New Zealand	A	1.43%	2013	1	0.81%	2.15%	76.47%	(188)	EC	EC	(189)	EC	EC
Nigeria	A	2.20%	2012	2	2.10%	2.50%	68.00%	EC	EC	EC	EC	PS	(190)
Norway	A	0.55%	2012	1	0.45%	0.70%	79.50%	(29)	(111)	(111)	(111)	PS	(111)
Oman	A	0.50%	2015	1	0.45%	--	75.00%	EC	(191)	E	(192)	EC	EC
Pakistan	A	4.80%	2007-2008	3	5.64%	9.66%	87.40%	(37)	EC	EC	(37)	PS	(193)
Panama	E	0.50%	2015	1	--	--	65.20%	EC	E	E	EX (179)	EX	(104)
Papua New Guinea	E	2.17%	2003-2005	2	--	13.80%	65.70%	(108)	E	(194)	EX (109)	EX	(136)
Peru	E	1.16%	2002*	2	--	--	80.00%	(195)	E	E	EX (179)	EX	(53)
Philippines	E	0.94%	2002-2004	2	0.33%	2.00%	78.00%	(196)	(196)	(197)	(196)	PS	(198)

Country	Prev. Est. Status	Anti-HCV Prevalence - Base	Study Year	Data Quality Score	Anti-HCV Prevalence - Low	Anti-HCV Prevalence- High	Percent Viraemic	Source (base)	Source (low)	Source (high)	Age source	Percent Viraemic Source Type	Percent Viraemic Source
Poland	A	0.86%	2009	2	0.59%	1.14%	70.00%	(199)	(199)	(199)	(200)	PS	(199)
Portugal	A	1.50%	1995	1	0.47%	2.87%	75.79%	(55)	(201)	(201)	(201, 202)	EX	(203-205)
Puerto Rico	E	2.30%	2005-2008	3	1.30%	4.20%	65.20%	(206)	(206)	(206)	(206)	EX	(104)
Qatar	A	1.98%	2008-2010	2	1.80%	2.20%	90.00%	(207)	(207)	(207)	(207)	NS	(207)
Romania	A	3.23%	2006-2008	3	2.94%	3.55%	85.00%	(208)	(105)	(105)	(208)	EC	EC
Russian Federation	A	4.10%	2010	2	1.16%	5.60%	71.00%	(61)	(209)	(210)	(61)	PS	(157)
Samoa	E	0.15%	2002	2	0.07%	0.40%	69.00%	(211)	(211)	(211)	EX (109)	EX	(5)
Saudi Arabia	A	0.51%	2011	1	0.60%	1.90%	70.00%	EC	(212)	(213)	(105)	PS	(214)
Slovakia	A	1.40%	2010-2011	3	0.88%	1.98%	49.23%	(29)	(215)	(215)	(29)	EC	(216)
Slovenia	A	0.40%	2015	1	0.30%	0.50%	78.30%	(105)	(105)	(105)	(217)	PS	(218)
South Africa	A	1.70%	2005	2	0.98%	2.48%	76.90%	(219)	(219)	(219)	(220)	EX	(221)
Spain	A	1.50%	2012	2	0.40%	2.64%	68.60%	EC	(222)	(204)	(223)	PS	(204)
Sweden	A	0.56%	2012	2	0.47%	0.69%	77.00%	(224)	(224)	(224)	(225)	PS	(225-227)
Switzerland	A	1.55%	1998	2	0.80%	1.75%	79.70%	(55, 228)	(229)	(228)	(230)	EC	(55)
Syrian Arab Republic	E	2.80%	2004	3	0.60%	--	87.50%	(231)	(45)	E	(231)	PS	(232)
China, Province of Taiwan	A	3.28%	1996-2005	2	2.50%	8.60%	74.40%	(233)	(234)	(235)	(234)	PS	(233)
Thailand	E	0.94%	2014	2	1.84%	3.66%	72.41%	(236)	(237)	(237)	(236)	PS	(236)
Tunisia	E	1.27%	1996	2	0.20%	1.70%	80.00%	(238)	(238)	(238)	(238)	PS	(238)
Turkey	A	0.95%	2009	3	0.60%	2.10%	82.00%	(239)	(240)	(241)	(239)	PS	(240)

Country	Prev. Est. Status	Anti-HCV Prevalence - Base	Study Year	Data Quality Score	Anti-HCV Prevalence - Low	Anti-HCV Prevalence- High	Percent Viraemic	Source (base)	Source (low)	Source (high)	Age source	Percent Viraemic Source Type	Percent Viraemic Source
United Arab Emirates	A	1.90%	2014	1	0.11%	--	68.00%	EC (105)	(242)	E	(105)	PS	(242)
United Kingdom of Great Britain and Northern Ireland	E	0.50%**	2005	2	0.40%	0.75%	68.70%	(243, 244)	(243)	(243)	(243)	PS	(245)
United States of America	E	1.48%	2003-2010	3	1.20%	2.40%	76.09%	(246)	(221)	(247)	(248)	PS	(246)
Uzbekistan	E	13.10%	1999-2000	2	6.40%	13.10%	39.24%	(23)	(23)	(23)	(23)	PS	(62)
Venezuela (Bolivarian Republic of)	E	1.06%	1999*	2	--	--	62.50%	(249)	E	(250)	(251)	PS	(249)
Viet nam	E	1.49%	2012	1	1.20%	2.00%	80.00%	EC	E	E	(252)	EC	EC
Yemen	E	1.30%	2010-2011	2	1.00%	1.99%	70.00%	(253)	(254)	(253)	(253)	EX	(214)

* Study year unavailable. Used publication year minus two; ** Estimate adjusted for total population; [1] Extrapolated from Cameroon; [2] Extrapolated from Ethiopia; A = approved: inputs and model outputs approved by country experts; E = Estimated: prevalence modeled & estimated using published data; EC = Expert Consensus; EX = Extrapolated; NS = National Surveillance System or Blood Donor database; PS = Published Study

Appendix 2: Inputs used to build and calibrate each country model.

Model input	Definition	Source
Country population by 5-year age cohort	The number of people in the country, reported annually from 1950 to 2050 (by gender and 5-year age cohort)	UN Database (255) or country specific database
Mortality rate by 5-year age cohort	The percent of deaths among the total population, annually from 1950 to 2050 (by gender and 5-year age cohort)	UN Database (255) or country specific database
Prevalence of serological evidence of past or present infection	Percent of total population who are anti-HCV(+)	See Appendix 1 for sources
Percent Viraemic	Percent of anti-HCV(+) individuals who are HCV-RNA(+)	See Appendix 1 for sources
Age and gender distribution	Prevalence of HCV infection by age (5 year cohorts) and gender	See Appendix 1 for sources
Genotype distribution	Proportion of HCV-RNA(+) population categorized by HCV genotype (out of 100%)	Estimates and sources published recently (41)
Annually treated	Number of HCV infected individuals who initiate treatment in a given year	National reports, published studies, drug sale data adjusted for average patient consumption by genotype
Total diagnosed	Viremic HCV cases diagnosed and alive in a given year	National registry or extrapolated
Newly diagnosed	Annual number of newly diagnosed HCV cases	National registry or extrapolated
Liver transplants	Annual number of liver transplants due to HCV	IRODaT (256) or the national registry adjusted for proportion attributed to HCV
HCC	Annual number of HCC incidence due to HCV	GLOBOCAN or national registry adjusted for proportion attributed to HCV

Appendix 3: Annual prevalence (total cases) calculations by stage, year and age

$$\text{Total Cases}_{\text{Stage}_x\ \text{Year}_y\ \text{Age Cohort}_z} = \text{Total Cases}_{\text{Stage}_x\ \text{Year}_{y-1}\ \text{Age Cohort}_{z-1}} + \text{New Cases}_{\text{Stage}_x\ \text{Year}_y\ \text{Age Cohort}_z} - \text{Cured}_{\text{Stage}_x\ \text{Year}_y\ \text{Age Cohort}_z} - \text{Background Mortality}_{\text{Stage}_x\ \text{Year}_y\ \text{Age Cohort}_z} - \text{Progressed}_{\text{Stage}_x\ \text{Year}_y\ \text{Age Cohort}_z} - \text{Liver Related Mortality}_{\text{Stage}_x\ \text{Year}_y\ \text{Age Cohort}_z}$$

where:

$$\text{New Cases}_{\text{Stage}_x\ \text{Year}_y\ \text{Age Cohort}_z} = \left(\text{Total Cases}_{\text{Stage}_{x-1}\ \text{Year}_{y-1}\ \text{Age Cohort}_{z-1}}\right)\left(\text{Progression Rate}_{\text{Stage}_{x-1}\rightarrow\text{Stage}_x\ \text{Age Cohort}_{z-1}}\right)$$

$$\text{Cured}_{\text{Stage}_x\text{Year}_y\text{Age Cohort}_z} = \left(\text{Total Cases}_{\text{Stage}_x\text{Year}_{y-1}\text{Age Cohort}_{z-1}}\right)\left(\text{Age Eligibility Flag}_{\text{Year}_{y-1}\text{Age Cohort}_{z-1}}\right)\left(\frac{\text{Cured}_{\text{Stage}_x\text{Year}_y}}{\text{Total Age Eligible Cases}_{\text{Stage}_x\text{Year}_{y-1}}}\right)$$

where:

$$\text{Cured}_{\text{Stage}_x\ \text{Year}_y} = \sum_{w=1}^{6}\left(\text{Total Treated}_{\text{Genotype}_w\ \text{Stage}_x\ \text{Year}_y}\right)\left(\text{SVR}_{\text{Genotype}_w\text{Year}_y}\right)$$

$$\text{Background Mortality}_{\text{Stage}_x\ \text{Year}_y\ \text{Age Cohort}_z} = \left(\text{Total Cases}_{\text{Stage}_x\ \text{Year}_{y-1}\ \text{Age Cohort}_{z-1}} - \text{Cured}_{\text{Stage}_x\text{Year}_y\text{Age}_z}\right)\left(\text{Adjusted Background Mortality Rate}_{\text{Year}_{y-1}\text{Age Cohort}_{z-1}}\right)$$

$$\text{Progressed}_{\text{Stage}_x\ \text{Year}_y\ \text{Age Cohort}_z} = \left(\text{Total Cases}_{\text{Stage}_x\ \text{Year}_{y-1}\ \text{Age Cohort}_{z-1}} - \text{Cured}_{\text{Stage}_x\text{Year}_y\text{Age Cohort}_z} - \text{Background Mortality}_{\text{Stage}_x\ \text{Year}_y\ \text{Age Cohort}_z}\right)\left(\text{Progression Rate}_{\text{Stage}_x\rightarrow\text{Stage}_{x+1}\ \text{Age Cohort}_{z-1}}\right)$$

$$\text{Liver Related Mortality}_{\text{Stage}_x\ \text{Year}_y\ \text{Age Cohort}_z} = \left(\text{Total Cases}_{\text{Stage}_x\ \text{Year}_{y-1}\ \text{Age Cohort}_{z-1}} - \text{Cured}_{\text{Stage}_x\text{Year}_y\text{Age Cohort}_z} - \text{Background Mortality}_{\text{Stage}_x\ \text{Year}_y\ \text{Age Cohort}_z} - \text{Progressed}_{\text{Stage}_x\ \text{Year}_y\ \text{Age Cohort}_z}\right)\left(\text{Liver Related Mortality Rate}_{\text{Year}_{y-1}\text{Age Cohort}_{z-1}}\right)$$

Progression rates – The progression rates by age, gender and fibrosis score were back calculated. Data from the UK were used for the percentage increase in progression rate by age and gender (257). However, this study only reported progression from chronic HCV to moderate chronic HCV and from moderated chronic HCV to cirrhosis. These reported rates were modified using a meta analysis of published work to calculate progression for F0, F1, F2, F 3 and F4 (32). Finally, the modified progression rates were adjusted to fit historical HCC incidence by age and gender in the US (31) after adjusting for the portion of all HCC cases attributed to HCC (30).

The progression rates to end stage liver disease and liver-related deaths were based on previously published rates. Insufficient data were available to develop predictable rates by age and gender. Thus, the same rate was applied for all ages and genders (257-259). The table below lists all progression rates along with the uncertainty intervals.

HCV disease progression rates

Back-Calculated Progression Rates – Males																		
Age Cohorts	**0-4**	**5-9**	**10-14**	**15-19**	**20-24**	**25-29**	**30-34**	**35-39**	**40-44**	**45-49**	**50-54**	**55-59**	**60-64**	**65-69**	**70-74**	**75-79**	**80-84**	**85+**
F0 to F1	5.3%	5.3%	5.3%	5.3%	5.3%	5.3%	5.3%	5.3%	13.9%	13.9%	17.1%	17.1%	19.4%	19.4%	21.8%	21.8%	21.8%	21.8%
Low	3.1%	3.1%	3.1%	3.1%	3.1%	3.1%	3.1%	3.1%	8.2%	8.2%	10.1%	10.1%	11.4%	11.4%	12.8%	12.8%	12.8%	12.8%
High	8.1%	8.1%	8.1%	8.1%	8.1%	8.1%	8.1%	8.1%	21.3%	21.3%	26.2%	26.2%	29.7%	29.7%	33.4%	33.4%	33.4%	33.4%
F1 to F2	3.4%	3.4%	3.4%	3.4%	3.4%	3.4%	3.4%	3.4%	9.1%	9.1%	11.2%	11.2%	12.7%	12.7%	14.3%	14.3%	14.3%	14.3%
Low	2.0%	2.0%	2.0%	2.0%	2.0%	2.0%	2.0%	2.0%	5.3%	5.3%	6.6%	6.6%	7.5%	7.5%	8.4%	8.4%	8.4%	8.4%
High	5.3%	5.3%	5.3%	5.3%	5.3%	5.3%	5.3%	5.3%	13.9%	13.9%	17.1%	17.1%	19.4%	19.4%	21.8%	21.8%	21.8%	21.8%
F2 to F3	5.4%	5.4%	5.4%	5.4%	5.4%	5.4%	5.4%	5.4%	14.3%	14.3%	17.5%	17.5%	19.9%	19.9%	22.4%	22.4%	22.4%	22.4%
Low	3.2%	3.2%	3.2%	3.2%	3.2%	3.2%	3.2%	3.2%	8.4%	8.4%	10.3%	10.3%	11.7%	11.7%	13.2%	13.2%	13.2%	13.2%
High	8.3%	8.3%	8.3%	8.3%	8.3%	8.3%	8.3%	8.3%	21.8%	21.8%	26.9%	26.9%	30.5%	30.5%	34.3%	34.3%	34.3%	34.3%
F3 to C Cirrhosis	5.7%	5.7%	5.7%	5.7%	5.7%	5.7%	5.7%	5.7%	9.3%	9.3%	9.3%	9.3%	10.4%	10.4%	20.0%	20.0%	20.0%	20.0%
Low	3.3%	3.3%	3.3%	3.3%	3.3%	3.3%	3.3%	3.3%	5.3%	5.3%	5.3%	5.3%	6.0%	6.0%	11.4%	11.4%	11.4%	11.4%
High	10.8%	10.8%	10.8%	10.8%	10.8%	10.8%	10.8%	10.8%	17.7%	17.7%	17.7%	17.7%	19.8%	19.8%	38.1%	38.1%	38.1%	38.1%
F3 to HCC	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%
Low	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%
High	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%
C Cirrhosis to Decomp	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%
Low	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%
High	4.1%	4.1%	4.1%	4.1%	4.1%	4.1%	4.1%	4.1%	4.1%	4.1%	4.1%	4.1%	4.1%	4.1%	4.1%	4.1%	4.1%	4.1%
C Cirrhosis to HCC	3.6%	3.6%	3.6%	3.6%	3.6%	3.6%	3.6%	3.6%	3.6%	3.6%	3.6%	3.6%	3.6%	3.6%	3.6%	3.6%	3.6%	3.6%
Low	2.7%	2.7%	2.7%	2.7%	2.7%	2.7%	2.7%	2.7%	2.7%	2.7%	2.7%	2.7%	2.7%	2.7%	2.7%	2.7%	2.7%	2.7%
High	4.8%	4.8%	4.8%	4.8%	4.8%	4.8%	4.8%	4.8%	4.8%	4.8%	4.8%	4.8%	4.8%	4.8%	4.8%	4.8%	4.8%	4.8%
Decomp to Death	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%
Low	16.0%	16.0%	16.0%	16.0%	16.0%	16.0%	16.0%	16.0%	16.0%	16.0%	16.0%	16.0%	16.0%	16.0%	16.0%	16.0%	16.0%	16.0%
High	24.0%	24.0%	24.0%	24.0%	24.0%	24.0%	24.0%	24.0%	24.0%	24.0%	24.0%	24.0%	24.0%	24.0%	24.0%	24.0%	24.0%	24.0%
HCC to Death (Yr 1)	70.7%	70.7%	70.7%	70.7%	70.7%	70.7%	70.7%	70.7%	70.7%	70.7%	70.7%	70.7%	70.7%	70.7%	70.7%	70.7%	70.7%	70.7%
Low	43.0%	43.0%	43.0%	43.0%	43.0%	43.0%	43.0%	43.0%	43.0%	43.0%	43.0%	43.0%	43.0%	43.0%	43.0%	43.0%	43.0%	43.0%
High	77.0%	77.0%	77.0%	77.0%	77.0%	77.0%	77.0%	77.0%	77.0%	77.0%	77.0%	77.0%	77.0%	77.0%	77.0%	77.0%	77.0%	77.0%
HCC to Death (Sub Yrs)	16.2%	16.2%	16.2%	16.2%	16.2%	16.2%	16.2%	16.2%	16.2%	16.2%	16.2%	16.2%	16.2%	16.2%	16.2%	16.2%	16.2%	16.2%
Low	11.0%	11.0%	11.0%	11.0%	11.0%	11.0%	11.0%	11.0%	11.0%	11.0%	11.0%	11.0%	11.0%	11.0%	11.0%	11.0%	11.0%	11.0%
High	23.0%	23.0%	23.0%	23.0%	23.0%	23.0%	23.0%	23.0%	23.0%	23.0%	23.0%	23.0%	23.0%	23.0%	23.0%	23.0%	23.0%	23.0%

Back-Calculated Progression Rates – Females																		
Age Cohorts	**0-4**	**5-9**	**10-14**	**15-19**	**20-24**	**25-29**	**30-34**	**35-39**	**40-44**	**45-49**	**50-54**	**55-59**	**60-64**	**65-69**	**70-74**	**75-79**	**80-84**	**85+**
F0 to F1	4.4%	4.4%	4.4%	4.4%	4.4%	4.4%	4.4%	4.4%	11.6%	11.6%	14.3%	14.3%	16.2%	16.2%	18.2%	18.2%	18.2%	18.2%
Low	2.6%	2.6%	2.6%	2.6%	2.6%	2.6%	2.6%	2.6%	6.8%	6.8%	8.4%	8.4%	9.5%	9.5%	10.7%	10.7%	10.7%	10.7%
High	6.7%	6.7%	6.7%	6.7%	6.7%	6.7%	6.7%	6.7%	17.7%	17.7%	21.8%	21.8%	24.8%	24.8%	27.8%	27.8%	27.8%	27.8%
F1 to F2	2.9%	2.9%	2.9%	2.9%	2.9%	2.9%	2.9%	2.9%	7.6%	7.6%	9.3%	9.3%	10.6%	10.6%	11.9%	11.9%	11.9%	11.9%
Low	1.7%	1.7%	1.7%	1.7%	1.7%	1.7%	1.7%	1.7%	4.5%	4.5%	5.5%	5.5%	6.2%	6.2%	7.0%	7.0%	7.0%	7.0%
High	4.4%	4.4%	4.4%	4.4%	4.4%	4.4%	4.4%	4.4%	11.6%	11.6%	14.3%	14.3%	16.2%	16.2%	18.2%	18.2%	18.2%	18.2%
F2 to F3	4.5%	4.5%	4.5%	4.5%	4.5%	4.5%	4.5%	4.5%	11.9%	11.9%	14.6%	14.6%	16.6%	16.6%	18.6%	18.6%	18.6%	18.6%
Low	2.6%	2.6%	2.6%	2.6%	2.6%	2.6%	2.6%	2.6%	7.0%	7.0%	8.6%	8.6%	9.8%	9.8%	11.0%	11.0%	11.0%	11.0%
High	6.9%	6.9%	6.9%	6.9%	6.9%	6.9%	6.9%	6.9%	18.2%	18.2%	22.4%	22.4%	25.4%	25.4%	28.6%	28.6%	28.6%	28.6%
F3 to C Cirrhosis	4.7%	4.7%	4.7%	4.7%	4.7%	4.7%	4.7%	4.7%	7.7%	7.7%	7.7%	7.7%	8.7%	8.7%	16.7%	16.7%	16.7%	16.7%
Low	2.7%	2.7%	2.7%	2.7%	2.7%	2.7%	2.7%	2.7%	4.4%	4.4%	4.4%	4.4%	5.0%	5.0%	9.5%	9.5%	9.5%	9.5%
High	9.0%	9.0%	9.0%	9.0%	9.0%	9.0%	9.0%	9.0%	14.7%	14.7%	14.7%	14.7%	16.5%	16.5%	31.8%	31.8%	31.8%	31.8%
F3 to HCC	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%
Low	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%
High	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%
C Cirrhosis to Decomp	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%
Low	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%
High	4.1%	4.1%	4.1%	4.1%	4.1%	4.1%	4.1%	4.1%	4.1%	4.1%	4.1%	4.1%	4.1%	4.1%	4.1%	4.1%	4.1%	4.1%
C Cirrhosis to HCC	3.6%	3.6%	3.6%	3.6%	3.6%	3.6%	3.6%	3.6%	3.6%	3.6%	3.6%	3.6%	3.6%	3.6%	3.6%	3.6%	3.6%	3.6%
Low	2.7%	2.7%	2.7%	2.7%	2.7%	2.7%	2.7%	2.7%	2.7%	2.7%	2.7%	2.7%	2.7%	2.7%	2.7%	2.7%	2.7%	2.7%
High	4.8%	4.8%	4.8%	4.8%	4.8%	4.8%	4.8%	4.8%	4.8%	4.8%	4.8%	4.8%	4.8%	4.8%	4.8%	4.8%	4.8%	4.8%
Decomp to Death	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%
Low	16.0%	16.0%	16.0%	16.0%	16.0%	16.0%	16.0%	16.0%	16.0%	16.0%	16.0%	16.0%	16.0%	16.0%	16.0%	16.0%	16.0%	16.0%
High	24.0%	24.0%	24.0%	24.0%	24.0%	24.0%	24.0%	24.0%	24.0%	24.0%	24.0%	24.0%	24.0%	24.0%	24.0%	24.0%	24.0%	24.0%
HCC to Death (Yr 1)	70.7%	70.7%	70.7%	70.7%	70.7%	70.7%	70.7%	70.7%	70.7%	70.7%	70.7%	70.7%	70.7%	70.7%	70.7%	70.7%	70.7%	70.7%
Low	43.0%	43.0%	43.0%	43.0%	43.0%	43.0%	43.0%	43.0%	43.0%	43.0%	43.0%	43.0%	43.0%	43.0%	43.0%	43.0%	43.0%	43.0%
High	77.0%	77.0%	77.0%	77.0%	77.0%	77.0%	77.0%	77.0%	77.0%	77.0%	77.0%	77.0%	77.0%	77.0%	77.0%	77.0%	77.0%	77.0%
HCC to Death (Sub Yrs)	16.2%	16.2%	16.2%	16.2%	16.2%	16.2%	16.2%	16.2%	16.2%	16.2%	16.2%	16.2%	16.2%	16.2%	16.2%	16.2%	16.2%	16.2%
Low	11.0%	11.0%	11.0%	11.0%	11.0%	11.0%	11.0%	11.0%	11.0%	11.0%	11.0%	11.0%	11.0%	11.0%	11.0%	11.0%	11.0%	11.0%
High	23.0%	23.0%	23.0%	23.0%	23.0%	23.0%	23.0%	23.0%	23.0%	23.0%	23.0%	23.0%	23.0%	23.0%	23.0%	23.0%	23.0%	23.0%

Appendix 4: Scores to assess the quality of data on the prevalence of HCV infection

HCV Prevalence Studies were scored on a scale of 0-10, following the approach described previously (5). This system was based on three metrics, which accounted for 60% (generalizability), 20% (sample size) and 20% (year of analysis) of the overall score, respectively:

Overall Score = 60% * Generalizability Score + 20% * Sample Size Score +

20% * Year of Analysis Score

Generalizability Score: The table below indicates the criteria used to score articles on their ability to be generalized to the total population.

Geographic Scope	**Scale, 0–10**				
					10†
National	0	3	4 Meta analysis - 4	6	9 Model - 6 Meta analysis - 5
Large Region Multi-Region Multi-City Large City	0	1	2-3‡	4-5‡	6-8‡
Small Region/Town Village Tribe Hospital	0	0	1	1	2
Population →	***High risk, any sampling method*** - ***IVDUs*** - ***HIV*** - ***Surgical patients***	***Healthy adults, self-selected*** - ***Blood donors***	***Healthy adults, self-selected*** - ***Health check-up patients*** - ***Screening***	***Healthy adults, randomly selected*** - ***Health care workers*** - ***Pregnant women*** - ***Soldiers***	***General population, randomly selected***

†10 reserved for a nationally representative sample with a stratified, multistage and random sampling design that documents the study design and demographics of subjects thoroughly (e.g. NHANES).
‡Variability subject to author's discretion based on quality of study design, as well as the geographic scope of the respective country.

Sample Size Score: The log of sample size was scaled to 0-10 whereby all studies with a samples size greater than 10,000 received a score of 10.

Year of the Analysis Score: Study year was assessed so that analyses conducted after 2010 received a score of 10, 2004-2010 a score of 8 and 2000-2003 a score of 6.

For simplicity, the 0-10 scores were converted to a data quality scale of 1-3, where an overall score of 0.0 < 4.0 received a data quality score of 1, 4.0 < 8.0 received a score of 2 and 8.0 < 10.0 received a score of 3. Modelling studies were automatically given a data quality score of 2. Studies without a formal assessment, but deemed to be of quality for inclusion, were given a score of 1.

Expert Consensus was assigned a default score of 1, unless supportive data were available. Expert consensus estimates based on supporting data were scored as follows: 2 = expert input based on published or unpublished data; 3 = expert consensus based on well conducted studies ahead of print and/or large national databases.

Results: The distribution of the countries analyzed is shown below.

Geographic Scope	Scale, 0–10				
					n = 4
National	n = 0	n = 0	n = 4 Meta-Analysis: n = 1	n = 3	n = 11 Model: n = 3 Meta-Analysis: n = 0
Large Region **Multi-Region** **Multi-City** **Large City**	n = 0	n = 0	n = 5	n = 10	n = 14
Small Region/Town **Village** **Tribe** **Hospital**	n = 0	n = 0	n = 0	n=0	n = 4
Population →	***High risk, any sampling method*** -***IVDUs*** -***HIV*** -***Surgical patients***	***Healthy adults, self-selected*** -***Blood donors***	***Healthy adults, self-selected*** -***Health check-up patients*** -***Screening***	***Healthy adults, randomly selected*** -***Health care workers*** -***Pregnant women*** -***Soldiers***	***General population, randomly selected***

The following countries had a representative national survey study with sampling in multiple regions of the country: Brazil, Cameroon, Egypt, France, Georgia, Indonesia, Iraq, Libya, Mexico, Mongolia, Pakistan, Romania, Syria, Turkey and United States. Other noteworthy countries were China, which conducted a nationwide HBV survey and the samples were later tested for HCV. Burundi conducted a nationwide HIV survey and the samples were later tested for HCV. Central African Republic also conducted a national survey but the results were provided in an abstract only. Greece conducted a phone survey to estimate prevalence of HCV infection. Slovakia completed the EPID study, but the results have not been published yet.

The quality score for expert consensus data is shown below. As described above, the default score was 1 unless supportive data was provided.

Expert Consensus

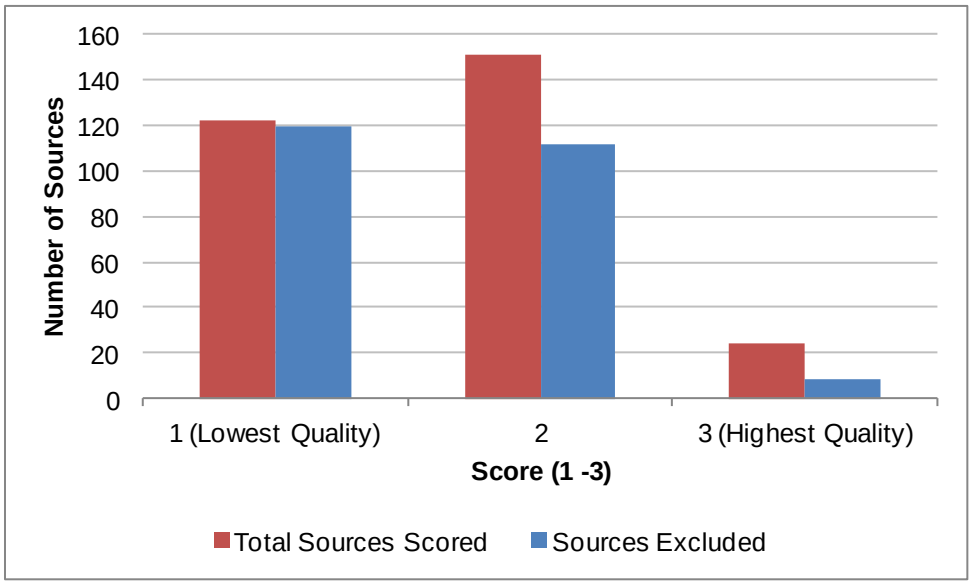
Quality Score (Scale 0-3)	1	2	3	Total
Approved Countries	**20**	**13**	**1**	**34**
Estimated Countries	**6**	**1**	**0**	**7**

Appendix 5: Studies excluded

In total, 297 studies were scored on a 1 (lowest) to 3 (highest) quality scale. Some studies were scored multiple times for various populations – (i.e. a study of pregnant women and children may be scored once for pregnant women and once for children).

In countries with a national study- after identifying a national study within a country (US, France, Egypt, Pakistan, Libya, Iraq), the search was stopped to ease the scoring burden, (i.e. there may be hundreds of studies in the US that report HCV prevalence in specific jurisdictions, but NHANES is widely recognized as the gold standard in the US).

In countries lacking data - an exhaustive search was run but studies in special populations that are not representative of the general population were ignored (i.e. blood donors, injection drug users, hemodialysis patients, etc).



Studies scoring a 3 that were excluded, and the rationale for exclusion

Country	Study	Rationale
1. Argentina	(53)	More recent consensus statement suggests a different prevalence rate, considering the results from this paper among others
2. Egypt	(260)	Reports the same data as the 2009 national study (261), which was use in conjunction with the 2015 national study (33)
3. Germany	(119)	Considered but not independently included – age distribution shows no cases under 40 years of age, which contradicts data from RKI, so this study was taken in consideration with other data
4. Korea, Republic of	(161)	Considered but not independently included
5. Mongolia	(181)	Considered but not independently included
6. Morocco	(185)	More recent Ministry of Health Study available (182)
7. United States	(221)	Reports similar data as the study chosen (246)
8. United States	(262)	Reports similar data as the study chosen (246)

Appendix 6: Description of the modified Delphi process used to review national estimates of the prevalence and incidence of HCV infection

		Activities
Phase 1 – Data Gathering	1a	**Identify country experts who are willing to collaborate** • Experts were identified through HCV-related scientific contributions, or through referrals and recommendations from leading researchers. Panels consisted of hepatologists, gastroenterologists, virologists, infectious disease specialists, epidemiologists, health economists, health scientists and Ministry of Health representatives
	1b	**Literature Search** • Review the internal database for previously identified sources • Review online sources (MOH, WHO, etc.) to capture non-indexed sources • Run a literature search from 2013 forward to identify recent publications • Summarize input data available through the literature • Gather empirical data for new HCC cases, liver transplants (LT), percent of HCC and LT due to HCV, annual newly diagnosed, annual treated, percent of infection due to transfusion and percent of infections that are among active PWID • Build draft model based on published data or extrapolate inputs from countries with data when data are missing (as a placeholder) • Schedule meeting with experts
Phase 2 – Country Meetings and Modelling	2a	**Expert Meeting 1 (2-3 hours)** • Provide a background on the project, model and methodology • Review data identified in Phase 1b and highlight gaps in data • Request data in local non-indexed journals, unpublished data and any other available data (e.g., hospital-level data) that can be used to fill the gaps • Gain agreement on countries that can used as for extrapolation when no local data are available
	2b	**Follow up with Experts Post Meeting 1** • Send minutes of the meeting and list of remaining action items to experts • Follow up with experts to collect missing data and get copies of publications in the local journals, unpublished data, relevant Ph.D. theses, government reports and raw hospital or registry-level data • Analyze raw data and send to experts for approval
	2c	**Disease Burden Modelling** • Populate disease burden model with inputs and calibrate model to empirical data • Develop 2-3 scenarios to prepare for meeting 2, including a WHO target scenario (elimination by 2030) • Schedule second meeting • Develop a slide deck summarizing all inputs and associated data sources • Perform a final check of the model and slide deck and approve internally
	2d	**Expert Meeting 2 (2-3 hours)** • Review all inputs as well as data provided by experts since meeting 1 and results of analyses of any raw data provided • Gain agreement on all inputs to be used in the model • Update the model using any updated inputs • Run scenarios requested by experts (e.g., slow increase in the number of treated patients, disease control, WHO target) and review results and insights • Agree on final strategies that would be considered as part of a national strategy
Phase 3 – Follow-up Analyses	3a	**Follow-up Analyses** • Update model as necessary and send results to experts • Provide support to address follow-up questions • Lock down inputs and outputs as approved • Run additional scenarios to support the development of a national strategy (e.g., economic impact, birth cohort screening and sources of transmission) • Report results to Polaris Observatory • Update analysis as new information becomes available (e.g., new national studies, updated treatment data)

Appendix 7: Flow of the Markov model used to estimate the prevalence of HCV infection in 2015 in each country.