Historical epidemiology of hepatitis C virus in select countries—volume 4

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Abbreviations: G, genotype; HCV, hepatitis C virus; IDU, injection drug use; Peg-IFN, Pegylated interferon; RBV, ribavirin; RNA, ribonucleic acid; UN, United Nations.

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Introduction

The hepatitis C virus (HCV) is of particular public health importance due to its influence on liver-related morbidity and mortality. As the infected population ages, increased rates of late-stage liver disease place a substantial burden on healthcare systems. With the introduction of pan-genotypic and high efficacy treatments, countries can cure and potentially eliminate HCV. However, country-specific epidemiological contexts vary, highlighting the need for tailored treatment and screening programs to reduce the disease burden. Low- and middle-income countries in particular often lack the surveillance systems and data needed to inform these policies. This analysis aims to address this need by providing country-level assessments of HCV-infected populations and related morbidity and mortality. Disease progression models were populated with data from the best available published and unpublished sources to estimate total number of viraemic infections, total number diagnosed, newly diagnosed and treated and liver transplants attributable to HCV. This analysis includes the results from modelling efforts in 17 countries and serves as a continuation of previous efforts to quantify HCV epidemiology globally.

Methodology

First, a systematic review of the literature was conducted to identify studies reporting the total number of HCV cases diagnosed, treated and cured in each country of interest. The review encompassed all studies published between January 1990 and September 2016. PubMed and EMBASE were queried for indexed articles, while nonindexed sources were identified through Ministry of Health websites and international agency reports. In addition, an expert panel in each country provided sources such as unpublished data and reports.

When no input data were available, analogues (data from countries with a similar demographic, risk factors and/or healthcare practices) were used. Lastly, in-person meetings were conducted to review findings with the expert panel. Uncertainty intervals were calculated for all inputs, with wider ranges implying greater uncertainty.

The term “viraemic” was used throughout this study to highlight chronic infections with the presence of HCV virus (RNA-positive infections). The term incidence was used to indicate new infections per year (acute or infections among immigrants entering the county) and not newly diagnosed. Year of data collection was also included. As shown in the next publication in this supplement, a modelling approach was used to estimate the HCV-infected populations (viraemic, diagnosed and treated) in 2015. Unless otherwise stated, population data were obtained from the United Nations (UN) population database by single-year age and gender cohorts.

The annual number of liver transplants was collected from national or international databases and adjusted for the proportion attributed to HCV. The number of antibody-positive (anti-HCV) and RNA-positive diagnosed cases was gathered from national databases, use of analogues or expert panel consensus. In countries where HCV was a notifiable infection and a reliable annual number of newly diagnosed cases was reported, the total number of diagnosed cases was calculated by summing data from all years after taking into consideration the mortality among the diagnosed cases. In countries

Summary

Due to the introduction of newer, more efficacious treatment options, there is a pressing need for policy makers and public health officials to develop or adapt national hepatitis C virus (HCV) control strategies to the changing epidemiological landscape. To do so, detailed, country-specific data are needed to characterize the burden of chronic HCV infection. In this study of 17 countries, a literature review of published and unpublished data on HCV prevalence, viraemia, genotype, age and gender distribution, liver transplants and diagnosis and treatment rates was conducted, and inputs were validated by expert consensus in each country. Viraemic prevalence in this study ranged from 0.2% in Hong Kong to 2.4% in Taiwan, while the largest viraemic populations were in Nigeria (2.597 million cases) and Taiwan (569,000 cases). Diagnosis, treatment and liver transplant rates varied widely across the countries included in this analysis, as did the availability of reliable data. Addressing data gaps will be critical for the development of future strategies to manage and minimize the disease burden of hepatitis C.

Key words
diagnosis, disease burden, epidemiology, HCV, hepatitis C, historical, incidence, mortality, prevalence, treatment
where the number of total and newly diagnosed cases was not available through surveillance data, national reports or expert panel input was used. Diagnosis rates from countries with empirical data were provided to the expert panel, and the panel selected one or more countries that had similar profiles. It was assumed that the viraemic rate among the diagnosed population was the same as the total infected population.

Two methods were used to estimate the total number of treated HCV patients. In countries where reliable national data were available, the reported numbers were used. In other countries, the annual number of units of pegylated interferon (Peg-IFN), ribavirin (RBV) or direct acting antivirals (DAAs) sold, as reported by IMS Health, were converted to treated patients using the average number of units per patient. The average number of units per patient was calculated using the genotype distribution of the infected population (assuming the genotype distribution of the treated population was the same as the overall population), the duration of treatment for each genotype, the number of Peg-IFN or RBV units per week and the per cent of patients who completed their treatment (80% in most countries unless stated otherwise). The annual number of units was adjusted using inputs from the expert panel to account for uses other than HCV as well as potential underreporting. Where these data were not available, expert consensus estimates were applied.

3 | RESULTS

Table 1 includes the results of the literature review for all 17 countries in this analysis, including estimates of antibody and viraemic prevalence, genotype distribution, viraemic diagnosis, annual treatment and liver transplants. The specific age and gender distribution of the viraemic prevalent population for each country are shown in Figure 1.

3.1 | Bahrain

3.1.1 | HCV-infected population

The prevalence of anti-HCV in the total population was 1.7% (1.0%-1.9%) in 2011. With a viraemic rate of 77%, the viraemic population in 2011 was estimated at 16 900 (10 000-18 900) individuals, corresponding to a viraemic prevalence of 1.3% (0.8%-1.5%). The age distribution was developed using analogue data from Saudi Arabia and was validated and modified by Bahraini experts to reflect a plateauing prevalence rate among the 60+ population. The gender distribution was applied from a study of the military medical academy in Sofia. The majority of cases were Genotype 1b (62.4%), followed by Genotype 1a (20%) and Genotype 3 (14%).

3.1.2 | Diagnosed

It was estimated that 280 new patients have been diagnosed annually for the last 10 years and that 2800 are diagnosed overall based on analogue data from Saudi Arabia.

3.1.3 | Treated

It was estimated that 100 patients were treated annually until 2014 when 50 were treated annually based on expert consensus.

3.1.4 | Liver transplants

Liver transplants are not performed in Bahrain; however, patients who are sponsored or can afford to pay may receive a transplant abroad. This practice has been increasing since 2007 and, according to expert input, there were 44 liver transplants performed in 2015, with 55% related to HCV.

3.2 | Bulgaria

3.2.1 | HCV-infected population

According to expert consensus, the anti-HCV prevalence in Bulgaria was 1.5% (0.7%-2.3%) in 2012. Applying a viraemic rate of 87%, the viraemic prevalence was estimated to be 1.3% (0.6%-2.0%), or 95 000 (44 300-146 000) viraemic cases. The age distribution came from a study of 865 patients at four outpatient clinical laboratories, in which the prevalence was highest among 30- to 39-year-olds. It was estimated that 53% of cases were male. The genotype distribution was informed by two sources: the distribution of patients treated through the National Health Insurance Fund and a study on the genotypes of patients at the Military Medical Academy in Sofia. The majority of cases were Genotype 1a (20%) and Genotype 1b (62.4%), followed by Genotype 3 (14%).

3.2.2 | Diagnosed

The number of newly diagnosed patients was estimated based on the average number of patients diagnosed at each of the 15 reference centres in Bulgaria. Based on expert input, it was estimated that there was an average of 80 patients diagnosed annually at each centre. The total number of diagnosed patients was estimated to be 18 000 in 2014 based on the assumption that there were 1200 patients diagnosed annually for the past 15 years.

3.2.3 | Treated

Treatment data, provided by expert input, came from the National Health Insurance Fund in Bulgaria. In 2015, a total of 720 patients were treated: 470 with Peg-IFN, 70 with triple therapies and 180 with DAA therapies. After March 1, 2016, all patients were treated with all-oral DAAs.
| Country’s population (000) | Bahrain | Bulgaria | Cameroon | Colombia | Croatia | Dominican Republic | Ethiopia | Ghana |
|---------------------------|---------|----------|----------|----------|---------|------------------|---------|-------|
| Year                      | 2011    | 2012     | 2011     | 2011     | 2013    | 2014             | 2014    | 2014  |
| Total cases               | 22      | 109      | 218      | 488      | 39      | 104              | 530     | 531   |
| (12.9 - 24.6)             | (50.9 - 167) | (169 - 232) | (390 - 610) | (29.3 - 48.8) | (85.5 - 253) | (331 - 662) | (426 - 1955) |       |
| Prevalence                | 1.7%    | 1.5%     | 1.0%     | 1.1%     | 0.9%    | 1.0%             | 1.0%    | 1.0%  |
| (1.0% - 1.9%)             | (0.7% - 2.3%) | (0.8% - 1.1%) | (0.9% - 1.4%) | (0.7% - 1.1%) | (0.8% - 2.4%) | (0.6% - 12.2%) | (1.2% - 5.5%) |       |
| Year of estimate          | 2011    | 2012     | 2011     | 2013     | 2014    | 2014             | 1994    | 2014  |
| Total viremic infections (000) | 16.9 | 95      | 163      | 390      | 27.3    | 68.1             | 397     | 395   |
| (10 - 18.9)               | (44.3 - 146) | (127 - 174) | (312 - 488) | (20.5 - 34.2) | (55.8 - 165) | (248 - 497) | (308 - 930) |       |
| Viremic prevalence        | 1.3%    | 1.3%     | 0.8%     | 0.9%     | 0.6%    | 0.6%             | 0.7%    | 1.5%  |
| (0.8% - 1.5%)             | (0.6% - 2.0%) | (0.7% - 1.1%) | (0.5% - 0.8%) | (0.5% - 1.6%) | (0.5% - 0.9%) | (0.9% - 4.1%) |       |
| Viremic rate               | 77%     | 87%      | 75%      | 80%      | 70%     | 65%              | 75%     | 74%   |
| Year of estimate          | 2011    | 2012     | 2003     | 2013     | 2015    | 2014             | 1994    | 2014  |
| Genotypes                 |         |          |          |          |         |                  |         |       |
| 1a                        | 14%     | 20%      | -        | 14%      | 13%     | 59%              | 9%      | -     |
| 1b                        | 21%     | 62%      | -        | 70%      | 37%     | 19%              | 3%      | 65%   |
| 1 other                   | 2%      | -        | 5%       | -        | 8%      | 4%               | 2%      | -     |
| 1 total                   | 37%     | 82%      | 40%      | 89%      | 59%     | 82%              | 14%     | 65%   |
| 2                         | 4%      | 1%       | 20%      | 5%       | 2%      | 10%              | 14%     | 34%   |
| 3                         | 16%     | 14%      | -        | 2%       | 36%     | 1%               | 10%     | -     |
| 4                         | 25%     | 1%       | 40%      | 4%       | 3%      | 0%               | 60%     | -     |
| 5                         | -       | -        | -        | -        | -       | -                | -       | -     |
| 6                         | -       | -        | -        | -        | -       | -                | -       | -     |
| Other                     | 19%     | 2%       | -        | -        | -       | 8%               | 4%      | 1%    |
| Year of estimate          | 2015    | 1991-2013| 2015     | 1991-2013| 1996-2005| 1991-2013        | 2015    | 2001  |
| Diagnosed (viremic)       |         |          |          |          |         |                  |         |       |
| Total cases               | 2800    | 18 000   | 11 400   | 47 600   | 6400    | 6900             | 19 900  | 27 700 |
| Annual newly diagnosed    | 280     | 1200     | 110      | 3200     | 150     | 690              | 2000    | 2800  |
| Year of estimate          | 2014    | 2014     | 2010     | 2014     | 2015    | 2015             | 2014    | 2014  |
| Treated & cured           |         |          |          |          |         |                  |         |       |
| Annual number treated     | 50      | 720      | 500      | 1000     | 150     | 265              | 2000    | 20    |
| Year of estimate          | 2015    | 2015     | 2015     | 2012     | 2015    | 2015             | 2015    | 2015  |
| Liver transplants         |         |          |          |          |         |                  |         |       |
| Total liver transplants   | 44      | 16       | 0        | 222      | 150     | 6                | 0       | 0     |
| HCV liver transplants     | 24      | 3        | 0        | 44       | 45      | 2                | 0       | 0     |
| % due to HCV              | 55%     | 17%      | 0%       | 20%      | 30%     | 40%              | 0%      | 0%    |
| Year of estimate          | 2015    | 2015     | 2015     | 2015     | 2015    | 2014             | 2014    | 2015  |
| Country's population (000) | Hong Kong | Jordan | Kazakhstan | Malaysia | Morocco | Nigeria | Oman | Qatar | Taiwan |
|---------------------------|-----------|--------|------------|----------|---------|---------|------|-------|--------|
|                           | 7200      | 6800   | 15 200     | 27 800   | 34 400  | 143 000 | 4200 | 280   | 23 300 |
| Year                      | 2013      | 2011   | 2013       | 2009     | 2015    | 2013    | 2015 | 2009  | 2012   |
| HCV antibody positive (000) |           |        |            |          |         |         |      |       |        |
| Total cases               | 20        | 28.4   | 439        | 523      | 413     | 3820    | 20.8 | 1.6   | 765    |
| (5.7 - 35.8)              | (6.8 - 37.3) | (411 - 550) | (392 - 653) | (345 - 605) | (3646 - 4340) | (18.7 - 27.3) | (0.6 - 6.1) | (583 - 2005) |
| Prevalence                | 0.3%      | 0.4%   | 2.9%       | 1.9%     | 1.2%    | 2.2%    | 0.5% | 0.6%  | 3.3%   |
| (0.1% - 0.5%)             | (0.1% - 0.6%) | (2.7% - 3.6%) | (1.4% - 2.4%) | (1.0% - 1.8%) | (2.1% - 2.5%) | (0.5% - 0.7%) | (0.2% - 2.2%) | (2.5% - 8.6%) |
| Year of estimate          | 2013      | 2011   | 2013       | 2009     | 2015    | 2013    | 2015 | 2009  | 2012   |
| Total viremic infections (000) |           |        |            |          |         |         |      |       |        |
| Total viremic cases       | 15.5      | 24     | 329        | 386      | 309     | 2597    | 15.6 | 1.5   | 569    |
| (4.4 - 27.8)              | (5.7 - 31.5) | (308 - 413) | (290 - 483) | (259 - 454) | (2479 - 2951) | (14 - 20.5) | (0.6 - 5.5) | (434 - 1492) |
| Viremic prevalence        | 0.2%      | 0.4%   | 2.2%       | 1.4%     | 0.9%    | 1.5%    | 0.4% | 0.5%  | 2.4%   |
| (0.1% - 0.4%)             | (0.1% - 0.5%) | (2.0% - 2.7%) | (1.0% - 1.7%) | (0.8% - 1.3%) | (1.4% - 1.7%) | (0.3% - 0.5%) | (0.2% - 2.0%) | (1.9% - 6.4%) |
| Viremic rate              | 78%       | 85%    | 80%        | 74%      | 75%     | 68%     | 75%  | 90%   | 74%    |
| Year of estimate          | 2013      | 2011   | 2013       | 2009     | 2015    | 2011    | 2015 | 2009  | 2012   |
| Genotypes                 |           |        |            |          |         |         |      |       |        |
| 1a                        | 4%        | 23%    | 3%         | -        | 6%      | -       | 5%   | 7%    | 3%     |
| 1b                        | 62%       | 19%    | 59%        | -        | 40%     | -       | 29%  | 40%   | 46%    |
| 1 other                   | -         | -      | -          | -        | 36%     | -       | -    | 10%   | 14%    |
| 1 total                   | 67%       | 42%    | 62%        | 36%      | 47%     | 79.4%   | 44%  | 61%   | 49%    |
| 2                         | 3%        | -      | 8%         | 1%       | 42%     | 5.9%    | 2%   | 2%    | 40%    |
| 3                         | 3%        | -      | 30%        | 62%      | 1%      | 7.4%    | 36%  | 10%   | 1%     |
| 4                         | -         | 58%    | -          | 1%       | 1%      | 4.4%    | 12%  | 26%   | 0%     |
| 5                         | -         | -      | -          | 0%       | -       | -       | -    | -     | -      |
| 6                         | 27%       | -      | 0%         | 0%       | 10%     | -       | 6%   | -     | 10%    |
| Other                     | -         | 0%     | -          | 0%       | 10%     | -       | -    | -     | -      |
| Year of estimate          | 1998-2009 | 2015   | 2013       | 2003-2013 | 2009    | 2011    | 2015 | 2015  | 2000-2002 |
| Diagnosed (viremic)       |           |        |            |          |         |         |      |       |        |
| Total cases               | 3400      | 4800   | 50 000     | 28 800   | 30 900  | 130 000 | 2300 | 600   | 222 000 |
| Annual newly diagnosed    | 370       | 480    | 4000       | 2900     | 3100    | 1300    | 230  | 100   | 16 400  |
| Year of estimate          | 2015      | 2014   | 2014       | 2014     | 2015    | 2015    | 2010 | 2015  | 2010   |
| Treated & cured           |           |        |            |          |         |         |      |       |        |
| Annual number treated     | 220       | 150    | 1800       | 540      | 3000    | 300     | 70   | 130   | 8000   |
| Year of estimate          | 2014      | 2015   | 2013       | 2012     | 2015    | 2012    | 2014 | 2014  | 2015   |
| Liver transplants         |           |        |            |          |         |         |      |       |        |
| Total liver transplants   | 59        | 18     | 50         | 1        | 8       | 0       | 28   | 26    | 503    |
| HCV liver transplants     | 4         | 2      | 14         | 0        | 6       | 0       | 10   | 13    | 96     |
| % due to HCV              | 6%        | 11%    | 28%        | 0%       | 75%     | 0%      | 36%  | 50%   | 19%    |
| Year of estimate          | 2015      | 2015   | 2016       | 2013     | 2015    | 2015    | 2015 | 2015  | 2011   |

Anti-HCV prevalence: prevalence of past or active HCV infection; viraemic prevalence: prevalence of active HCV infections; viraemic rate: per cent of past or active infections who have an active infection; viraemic diagnosed: the number of individuals diagnosed with an active infection; annual newly diagnosed: the number of active HCV infections diagnosed for the first time.
**FIGURE 1** Viraemic hepatitis C virus (HCV) prevalence by age and gender

**FIGURE 1** (Continued)
3.2.4 | Liver transplants

Actual liver transplant data were available through the Republic of Bulgaria Ministry of Health Executive Agency for Transplantation. In 2015, 16 transplants were performed, 17% of which were due to HCV.

3.3 | Cameroon

3.3.1 | HCV-infected population

The prevalence of anti-HCV in the total population was estimated at 1.0% (0.8%-1.1%) based on unpublished data in individuals aged 15-59 years provided by expert input. These data were collected from a 2011 survey of 15,000 households stratified to provide adequate representation of urban and rural areas in the 10 administrative regions. A viraemic rate of 75% was applied. The total viraemic population in 2015 was estimated at 163,000 (127,000-174,000) individuals, corresponding to a viraemic prevalence of 0.8% (0.6%-0.8%). An age and gender distributions were constructed using the aforementioned data for HCV infection for individuals aged 15-59 years. The genotype distribution of the prevalent population was estimated using expert input.

3.3.2 | Diagnosed

Estimates of the diagnosed population were based on expert input. There were an estimated 11,400 previously diagnosed cases in 2010 and 110 newly diagnosed cases.

3.3.3 | Treated

It was estimated through expert input that at least 500 patients were treated with Peg-IFN/RBV or DAAs in 2015.

3.3.4 | Liver transplants

Currently, no liver transplants are performed in Cameroon due to resource and cost constraints. Almost all of those who need a liver transplant are unable to afford services abroad.

3.4 | Colombia

3.4.1 | HCV-infected population

In Colombia, there have not been any large-scale studies examining the prevalence of HCV among the general population. Recent blood bank data have shown an anti-HCV prevalence as low as 0.39%, while a study of high-risk populations (including sex workers, healthcare workers and indigenous peoples) reported a prevalence of 3.55%. Ultimately, expert opinion was utilized to estimate an anti-HCV prevalence of 1.1% (0.9%-1.4%) in 2013. As no country-specific data were available, a viraemic rate from Argentina of 80% was applied resulting in an estimated 390,000 (312,000-488,000) viraemic infections, corresponding to a viraemic prevalence of 0.9% (0.7%-1.1%) in 2013. Colombia implemented a national surveillance system in 2009, Sistema de Vigilancia en Salud Publica (SIVIGILA), which found the highest concentration of reported cases in those aged 40-60 years. The data...
from SIVIGILA were used to create an age and gender distributions that were then scaled up to match the prevalence. The genotype data from Colombia showed the predominant genotype as 1b at 70%.

3.4.2 | Diagnosed

In 2014, it was estimated that there were 47 600 individuals previously diagnosed with HCV, with 3200 diagnosed annually.

3.4.3 | Treated

In 2012, it was estimated that approximately 1000 individuals were treated for HCV with Peg-IFN.

3.4.4 | Liver transplants

In 2014, there were 222 liver transplants performed in Colombia. According to national data, approximately 20% of all liver transplants can be attributed to HCV, corresponding to 44 HCV-related liver transplants annually.

3.5 | Croatia

3.5.1 | HCV-infected population

HCV epidemiology data are sparse in Croatia. The prevalence of anti-HCV in the total population was estimated at 0.9% (0.7%-1.1%), and a viraemic rate of 70% was applied based on expert consensus. The total viraemic population in 2015 was estimated at 27 300 (20 500-34 200) individuals, corresponding to 44 HCV-related liver transplants annually.

3.5.2 | Diagnosed

Estimates of the diagnosed population were based upon expert consensus. Experts agreed that since diagnosis began in 1993, 300 patients were diagnosed per year until 2010, when diagnosis was scaled back to 200 patients per year. In 2015, 150 patients were diagnosed. In 2015, there were an estimated 6400 total diagnosed individuals.

3.5.3 | Treated

Experts agreed that 300 patients were treated annually from 2000 to 2012 but that this number dropped to 150 patients in 2013. DAAs were introduced in September of 2015 and approximately 150 patients were treated that year.

3.5.4 | Liver transplants

Experts agreed that in 2015, there were 150 liver transplants performed in Croatia; 45 (30%) were attributable to HCV. The annual number of liver transplants was available from the International Registry on Organ Donation and Transplantation (IRODaT) for the years 1999-2015. IRODaT only reports 141 liver transplants in 2015, but this nine-transplant discrepancy could be attributable to underreporting.

3.6 | Dominican Republic

3.6.1 | HCV-infected population

According to expert input, the anti-HCV prevalence in the Dominican Republic was 1.0% (0.8%-2.4%) in 2014. Applying a viraemic rate of 65.2% from Mexico, the viraemic prevalence was estimated to be 0.6% (0.5%-1.6%), or 68 100 (55 800-165 000) viraemic cases. Unpublished data from the national liver unit, provided by expert input, were used to create the age and gender distribution for 2013. According to these data, there was twice the amount of cases in women as there were in men, and the age group with the highest prevalence was 50- to 54-year-olds. According to a genotype distribution from the national liver unit, the majority of cases were estimated to be Genotype 1a.

3.6.2 | Diagnosed

The number of diagnosed patients was estimated using expert input. It was estimated that 6900 patients have been diagnosed in the Dominican Republic and that 690 patients were newly diagnosed in 2015.

3.6.3 | Treated

According to expert input, 265 patients were treated in 2015, 40 of whom received IFN-free therapies.

3.6.4 | Liver transplants

Actual liver transplant data were available from IRODaT for the years 2000 to 2014. In 2014, six liver transplants were performed in the Dominican Republic. It was estimated based on expert input that 40% of liver transplants were due to HCV.

3.7 | Ethiopia

3.7.1 | HCV-infected population

A 1994 population based study in Ethiopia identified an anti-HCV prevalence of 1.0% (0.6%-1.2%) in the general population. A viraemic rate of 75% was suggested in a prospective study of adult patients 18 years of age and older in two referral clinics in Addis Ababa. This
3.7.2 | Diagnosed

As of 2014, approximately 19,900 of the 397,000 viraemic cases (5%) were diagnosed (expert opinion). Approximately 2,000 chronic HCV cases were newly diagnosed in 2014 (expert opinion).

3.7.3 | Treated

In 2015, 2,000 patients were treated for HCV with Peg-IFN and RBV. It was estimated that approximately 10,000 patients have been treated over a five-year period, resulting in approximately 2,000 patients per year (expert consensus).

3.7.4 | Liver transplants

Currently, no liver transplants are performed in Ethiopia. If patients are eligible and have the funds, they may travel out of the country for the procedure (expert consensus).

3.8 | Ghana

3.8.1 | HCV-infected population

HCV epidemiology data in the general population are sparse in Ghana. The prevalence of anti-HCV was estimated at 2.0% (1.2%-5.5%) in 2014, based on unpublished data provided by Dr. Jennifer Layden of Loyola University Chicago, from an ongoing HCV prevalence study. A viraemic rate of 74% was applied. The total viraemic population in 2014 was estimated at 395,000 (308,000-930,000) individuals, corresponding to a viraemic prevalence of 1.5% (0.9%-4.1%). This study also provided the age and gender distribution of the infected population. The genotype distribution of the prevalent population was estimated using data from a population of almost 5,000 blood donors, with Genotype 1 being the predominant genotype.

3.8.2 | Diagnosed

Estimates of the diagnosed population were based on expert input. There were an estimated 27,700 previously diagnosed cases in 2014 and 2,800 newly diagnosed cases.

3.8.3 | Treated

It was estimated that at least 20 patients were under treatment in 2015 based on expert consensus and regional treatment rates.

3.8.4 | Liver transplants

Currently, liver transplants are not performed in Ghana due to resource and cost constraints. Almost all those who need a liver transplant are unable to afford services abroad.

3.9 | Hong Kong

3.9.1 | HCV-infected population

There have not been any large studies of HCV prevalence in the general population in Hong Kong. According to one study, the prevalence of HCV in blood donors is very low (0.035%-0.099%) and relatively low in hospital patients who are a high-risk group (0.8%). Based on this, experts estimated that approximately 0.3% (0.1%-0.5%) of the overall population is infected with HCV. The viraemic rate is estimated at 78% of all anti-HCV-positive cases. The total viraemic population in 2013 was estimated at 15,500 (4,400-27,800) individuals, corresponding to a viraemic prevalence of 0.2% (0.1%-0.4%). A Department of Health report of data from 2014 provided the age and gender breakdown of confirmed cases in Hong Kong, in which prevalence rates increase by age group and there are three times as many infections in males as there are in females. The genotype distribution from a study of 303 hospital patients was applied and modified using the Genotype 1 split between subtypes 1a and 1b from Zhou. Genotype 1 is the predominant genotype in Hong Kong.

3.9.2 | Diagnosed

Experts estimated that half of diagnosed cases are treated in Hong Kong, corresponding to 3,400 diagnosed cases and 370 newly diagnosed cases annually.

3.9.3 | Treated

Drug sales data were used to estimate that 220 patients were treated in 2014.

3.9.4 | Liver transplants

In 2015, there were 59 liver transplants performed in Hong Kong, and in accordance to unpublished data, an estimated 6% were attributable to HCV. The annual number of liver transplants was available from IRODaT for the years 1996 to 2015.

3.10 | Jordan

3.10.1 | HCV-infected population

A nationally representative study of 706 individuals in Jordan found an anti-HCV prevalence of 0.4% (0.1%-0.6%) in 2011, corresponding to a viraemic prevalence of 0.4% (0.1%-0.5%) or 24,000 (5700-31,500) cases when a viraemic rate of 85% from data in Lebanon was
Prevalence was highest in individuals between the ages of 30-40 years, according to data from a study of 8750 blood donors in Zarka, Jordan. Similar to many countries in the region, the prevalence was higher in men than in women. A study of genotype distribution found that Genotype 4 was the most prevalent in Jordan, followed by Genotype 1. The Genotype 1 subtype split was estimated using data from haemodialysis patients.

### 3.10.2 | Diagnosed

Data on the number of diagnosed patients in Jordan are scarce. Analogue data from Lebanon were used, where experts estimated that 20% (4800 cases) of the prevalent population had been diagnosed and 2% (480 cases) was newly diagnosed annually.

### 3.10.3 | Treated

Expert opinion was used to estimate that approximately 5000 patients were treated from 2006 to 2015 in public healthcare systems. The annual number treated has dropped in recent years, and an estimated 150 patients were treated in 2015.

### 3.10.4 | Liver transplants

It is reported that 18 transplants were performed per year from 2004 to 2013 with an estimated 11% related to HCV (unpublished data from Royal Medical Services). It is estimated that approximately 20 transplants are performed each year on average and specifically 18 in 2015 (expert input).

### 3.11 | Kazakhstan

#### 3.11.1 | HCV-infected population

In Kazakhstan, there are no national studies in the general population. A study conducted in the general population of Almaty in 2005 reported an anti-HCV prevalence of 3.2% among those aged 10-64 years. A separate study in South Kazakhstan was conducted in 2013 among those aged 18-69 years and reported an average anti-HCV prevalence of 3.9%. The age and gender distributions from South Kazakhstan were used while both studies were utilized to create a population weighted average anti-HCV prevalence of 2.9% (2.2%-3.6%) corresponding to 439 000 (411 000-550 000) infected individuals in 2013. There were no country-specific studies available regarding a viraemic rate, but a rate of 80% was agreed upon via expert consensus. This viraemic rate results in an estimated 329 000 (308 000-413 000) viraemic infected individuals, corresponding to a viraemic prevalence of 2.2% (2.0%-2.7%) in 2013. In 2009, a large-scale screening program was initiated in Kazakhstan with over 50 000 individuals captured in a patient registry by 2014. The genotype data from both unpublished registry data as well as a separate study found the predominant genotype as 1b at 59%.

#### 3.11.2 | Diagnosed

In 2014, it was estimated that there were 50 000 individuals previously diagnosed with HCV, with 4000 newly diagnosed annually (expert consensus).

#### 3.11.3 | Treated

In 2013, it was estimated that approximately 1800 individuals were treated for HCV, with the majority being treated with Peg-IFN (expert consensus).

#### 3.11.4 | Liver transplants

In 2016, there were 50 liver transplants performed in Kazakhstan. According to national data, approximately 28% of all liver transplants can be attributed to HCV, corresponding to 14 HCV-related liver transplants annually.

### 3.12 | Malaysia

#### 3.12.1 | HCV-infected population

HCV epidemiology data are sparse in Malaysia. The prevalence of anti-HCV in the total population was estimated at 1.9% (1.4%-2.4%). This number was calculated with data from two recent studies of patients 15-64 and 0-16 years of age, after adjusting for the population aged 65 years or older. A viraemic rate of 14% was applied. The total viraemic population in 2009 was estimated at 386 000 (290 000-483 000) individuals, corresponding to a viraemic prevalence of 1.4% (1.0%-1.7%). For the age and gender distribution of the infected population, HCV notification data from 2009 to 2014, as well as data from Hospital Selayang for 2000-2013, were used. The genotype distribution of the prevalent population was estimated using data from Hospital Selayang, which included genotype data on almost 700 patients. Genotype 3 was found to be the predominant genotype.

#### 3.12.2 | Diagnosed

There were an estimated 28 800 previously diagnosed cases in 2014 and 2900 newly diagnosed cases. Estimates of the diagnosed population were based upon notification data from the Ministry of Health Malaysia for the years 2003-2013, expert input was used for 2014. Since data were not available from 1993 to 2002, it was assumed that the total cases during this period remained the same as in 2003. To take into account underreporting, it was assumed that notified cases accounted for 50% of all diagnosed patients.

#### 3.12.3 | Treated

It was estimated that 540 patients were treated annually based on IMS data for standard units of Peg-IFN sold after adjustment to account for underreporting.
3.12.4 | Liver transplants

In 2013, there was one liver transplant performed in Malaysia; however, it was not attributable to HCV. The annual number of liver transplants was available from IRODaT for the years 2001-2010 and 2012-2013. The proportion of liver transplants attributable to HCV was reported as 0% based on expert input.

3.13 | Morocco

3.13.1 | HCV-infected population

The Ministry of Health in Morocco estimates the national anti-HCV prevalence to be 1.2% (1.0%-1.8%) in the general population in 2015. Applying a viraemic rate of 75%, the estimated viraemic prevalence in 2015 is estimated to be 0.9% (0.8%-1.3%) or 309 000 (259 000-454 000) cases. The age and gender distributions were determined using data from a nationwide study that was conducted between 2005 and 2011. According to the trends in this study, prevalence increased with age group, and there were more cases in females than males. The genotype distribution used in the model came from a study of 1473 HCV-positive individuals, in which the majority of patients were infected with Genotype 1 or Genotype 2.

3.13.2 | Diagnosed

It was estimated that approximately 10% of infected cases have been diagnosed (30 900) and that 3100 (~1%) were newly diagnosed in 2015 (expert input).

3.13.3 | Treated

According to expert input, 3000 patients were treated in 2015 and 47 000 patients received treatment between 1994 and 2014.

3.13.4 | Liver transplants

According to expert input, there were eight liver transplants in 2015, of which 75% were due to HCV.

3.14 | Nigeria

3.14.1 | HCV-infected population

The 2013 prevalence of anti-HCV in the total population was estimated at 2.2% (2.1%-2.5%) based on a Federal Ministry of Health study and expert consensus. A viraemic rate of 68% was applied. The total viraemic population in 2013 was estimated at 2 597 000 (2 479 000-2 951 000) individuals, corresponding to a viraemic prevalence of 1.5% (1.4%-1.7%). For the age and gender distribution of the infected population, the distribution reported in a study conducted between 2010 and 2012 was used. The genotype distribution of the prevalent population was estimated using data from a population of over 100 confirmed HCV-positive patients from across Nigeria and showed a Genotype 1 predominance. There were no studies identified that analysed HCV genotype subtypes in Nigeria.

3.14.2 | Diagnosed

Estimates of the diagnosed population were based on expert input. There were an estimated 130 000 previously diagnosed and 1300 newly diagnosed cases in 2013.

3.14.3 | Treated

It was estimated that at least 300 patients are treated annually based on expert input. However, it is believed that some patients may be treated outside of standard protocols.

3.14.4 | Liver transplants

Currently, no liver transplants are performed in Nigeria.

3.15 | Oman

3.15.1 | HCV-infected population

While there are no published data on the prevalence of anti-HCV in the general population in Oman, expert opinion estimated the prevalence at 0.5% (0.5%-0.7%) in 2015. This estimate considers studies of healthy blood donors and assumes the general population has a higher prevalence. With a viraemic rate of 75% (expert input), the viraemic population in 2015 was estimated at 15 600 (14 000-20 500) individuals, corresponding to a viraemic prevalence of 0.4% (0.3%-0.5%). The age and gender distributions were developed using clinical data of 603 patients with hepatitis C infection and was adjusted to the age and gender distribution in the general population. There was a slightly higher proportion of males (65.8%) than females, which is consistent with other countries in the region. The genotype distribution was based on the results of the same study, which found Genotype 1 to be the most prevalent (44%), followed by Genotype 3 (36%) and Genotype 4 (12%).

3.15.2 | Diagnosed

Expert input estimated that 15% (2300 cases) of the infected population has received a diagnosis and that 10% of those—230 patients—were diagnosed in 2010.

3.15.3 | Treated

Local clinicians estimated that between 30 and 35 patients were treated annually from 2004 to 2009, and 70 were treated in 2014.

3.15.4 | Liver transplants

Unpublished data from the Treatment Abroad Office database within the Ministry of Health report that starting in 2012, an annual average
of 28 patients underwent living donor-related liver transplantation abroad (India) and more than one-third of them were due to HCV.

3.16 | Qatar

3.16.1 | HCV-infected population

A representative study of Qatari national adults age 18-65 years found an anti-HCV prevalence of 0.8% in data collected from 2008 to 2010. These data were adjusted to all age groups for a prevalence estimate of 0.6% (0.2%-2.2%) in the general population, resulting in a viraemic prevalence of 0.5% (0.2%-2.0%) or 1550 (550-5500) cases when a viraemic rate of 90% from the same study was applied. Prevalence was highest in the oldest age group in the study (55-65 years) and, similar to many countries in the region, the prevalence was higher in men than in women. Unpublished clinical data were used to estimate the genotype distribution, which reported Genotype 1 as the most predominant type among Qatari nationals, followed by Genotype 4.

3.16.2 | Diagnosed

An estimated 100 new cases of HCV were diagnosed among nationals in 2015 (expert input). The Hamad Medical Corporation reported 1610 cases of HCV diagnosed in 2014 and unpublished data from the Supreme Health Council reported 9600 diagnosed cases\footnote{\textsuperscript{86}} over the last 10 years. Using the proportion of cases reported by HMC in one year to the cases reported in the last 10 years, there were an estimated 600 total cases diagnosed among nationals.

3.16.3 | Treated

According to expert input, there were more than 100 patients treated with new therapies in 2014, and the Hamad Medical Corporation reports there were 278 patients treated with Peg-IFN based therapies in 2014.\footnote{\textsuperscript{85}} According to expert input, Qatari nationals account for 85% of those treated with DAAs and 15% of those treated with older therapies in the country.

3.16.4 | Liver transplants

The first liver transplant was performed in Qatar in 2011\footnote{\textsuperscript{87}} and an average of 13 per year are performed on national HCV patients, according to unpublished data.

3.17 | Taiwan

3.17.1 | HCV-infected population

A national surveillance study found an anti-HCV prevalence of 3.3% (2.5%-8.6%) in Taiwan.\footnote{\textsuperscript{88}} The viraemic rate from the same study was found to be 74%, corresponding to a viraemic prevalence rate of 2.4% (1.9%-6.4%) or 569 000 (434 000-1 492 000) cases.\footnote{\textsuperscript{88}} Age and gender distributions were determined from Ministry of Health data on annually reported cases and show a slightly higher prevalence rate among males and increasing prevalence as age increases.\footnote{\textsuperscript{89}} Data on the genotype distribution, which was majority Genotype 1 and Genotype 2, came from an analysis of 418 HCV-infected patients in Kaohsiung Chang Gung Memorial Hospital.\footnote{\textsuperscript{90}}

3.17.2 | Diagnosed

According to unpublished data from the National Health Insurance Research Database, approximately 22 000 cases of anti-HCV are diagnosed annually. It is estimated by expert input that 40% (222 000 cases) of all cases of HCV have been diagnosed and that 16 400 viraemic cases (by applying the viraemic rate to 22 000) were newly diagnosed in 2010.

3.17.3 | Treated

IMS data for standard units of Peg-IFN sold were used to estimate the number of patients treated from 2003 to 2010.\footnote{\textsuperscript{27}} According to expert consensus, 8000 patients received treatment in 2015. From 2003 to 2014, a total of 80 000 patients were estimated to have received treatment.

3.17.4 | Liver transplants

Data on liver transplants were available through IRODaT for the years 1993-2011.\footnote{\textsuperscript{50}} In 2011, there were 503 liver transplants performed.\footnote{\textsuperscript{50}} An estimated 19% of liver transplants were attributable to HCV, according to unpublished data from the National Taiwan University Hospital.

4 | DISCUSSION

The recent introduction of WHO guidelines for the management of hepatitis B and C\footnote{\textsuperscript{81}} underscored a need for reliable baseline data. This analysis provides an overview of HCV epidemiology in countries where nationally representative data have historically been sparse. The results presented here add to a growing body of literature aimed at quantifying the HCV disease burden both nationally and globally. A standard methodology was used to identify studies and gain consensus around the HCV epidemiology for each country. The outcomes of this effort are summarized in Table 1. The next two manuscripts in this supplement build on the foundation of these data through disease burden forecasting and the development of management strategies.

Historical viraemic prevalence estimates varied across countries, ranging from 0.2% in Hong Kong to 2.4% in Taiwan. The reported prevalence distribution by age and gender also varied by country and was largely influenced by transmission route (Figure 1). Ongoing transmission through injection drug use was displayed through higher prevalence in young males, while historical transmission through traditional practices and an unsafe blood supply was seen in countries with an older infected population.

Genotype 1 was the most commonly reported genotype in the analysis. Bulgaria, Colombia and Dominican Republic specify more than 80%
Genotype 1, while another six countries reported rates of 50% or more. Genotype 3 was the most common in Malaysia, while Genotype 4 accounted for more than a quarter of infections in five countries (Bahrain, Cameroon, Ethiopia, Jordan and Qatar) and was the most common genotype in Ethiopia and Jordan. This variance in genotype distribution, even within regions, reflects the differences in current epidemiological situations and risk factors as previously discussed and holds important implications for treatment strategies at the country level.

During the analysis, economical and logistical barriers were identified in low- and middle-income countries. One example of this is that few countries involved in this analysis conduct liver transplants. Four countries do not perform liver transplants and 10 performed fewer than 10 HCV-related transplants per year. Some patients from Bahrain and Oman are able to receive transplants through partnerships with transplant centres abroad.

This study presents several limitations, the impact of which the authors have tried to mitigate. Inherent with any modelling effort, the data inputs were limited by the quality of the studies used. Prevalence estimates were reported with a confidence interval to capture the uncertainty surrounding estimates. In countries with limited or no available data, expert input was used, and in some cases, analogue data from similar data sources were applied.

The analysis utilized studies in the general or healthy adult population, which were sometimes limited in size and scope. This was particularly true for viraemic rate publications, where data were sparsely available for some African and Middle Eastern countries. When possible, the viraemic rate was chosen from the same study as the anti-HCV prevalence estimate. However, on occasion the source for viraemic rate and prevalence differed, in which case the expert panels carefully considered the testing landscape and time period to ensure appropriate comparison.

Data on number of treated patients were available through published literature, analysis of drug sales data or expert input. Because the treatment landscape is rapidly changing and national treatment registries do not exist in the countries analysed, these estimates may not capture all treated cases and thus may underestimate the true number of treated patients. The same issue presents itself with regard to diagnosis estimates, which relied heavily on analogue assumptions. This analysis identifies key data gaps in diagnosis and treatment estimates, suggesting a need for linked national screening and treatment registries. In order to implement strategies to achieve WHO recommendations, policymakers must have an understanding of the population level impact of HCV.

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