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# Editorial

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## Is screening baby boomers for HCV enough? A call to screen for hepatitis C virus in persons from countries of high endemicity

Hepatitis C virus (HCV) has a current global prevalence rate of approximately 2–3%, representing approximately 130–180 million infected individuals (1, 2). Persons chronically infected with HCV are at risk of chronic hepatitis and of developing serious hepatic complications such as cirrhosis, hepatocellular carcinoma (HCC), or liver failure.

Several data suggest that the prevalence of HCV is higher in countries located in Asia (2.1%, 83 millions) and Africa (3.2%, 28 millions), while a lower prevalence is found in North America, Europe and Australia (1, 2). (Fig. 1). The highest prevalence of HCV, 15%, is found in Egypt, while the lowest reported prevalences are <1.0% in both the UK and Scandinavia. However, only limited country-specific estimates of HCV prevalence are available to guide decision making.

In the USA and Europe, HCV is the leading cause of cirrhosis and hepatocellular carcinoma, and the major cause of end-stage liver disease leading to liver transplantation. Data from death certificates show that HCV-related deaths now outpace deaths because of HIV in the USA and many European countries (3, 4).

Despite progress in antiviral treatment with direct-acting antivirals (5), screening and access to treatment has been low. A recent report commissioned by the Institute of Medicine (IOM) of the National Academies estimates that up to 75% of HCV-infected persons have not been diagnosed (6).

Several HCV management guidelines have been provided (7–9) (Table 1). Prior risk-factor based HCV screening guidelines have demonstrated limited effectiveness, identifying only approximately 25% of chronically infected individuals in the USA. In an effort to identify more cases of HCV-infected persons, the CDC recently updated their screening guidelines to include one-time testing for all adults born during the period of 1945–1965 (9). Several studies suggest that HCV screening and treating among the 1945–1965 birth cohort at a prevalence of approximately 3% would be cost-effective (10, 11).

Despite the differences in geographical distribution of HCV prevalence worldwide, there are currently no recommendations in the USA or Europe to screen persons who originate from countries with high HCV

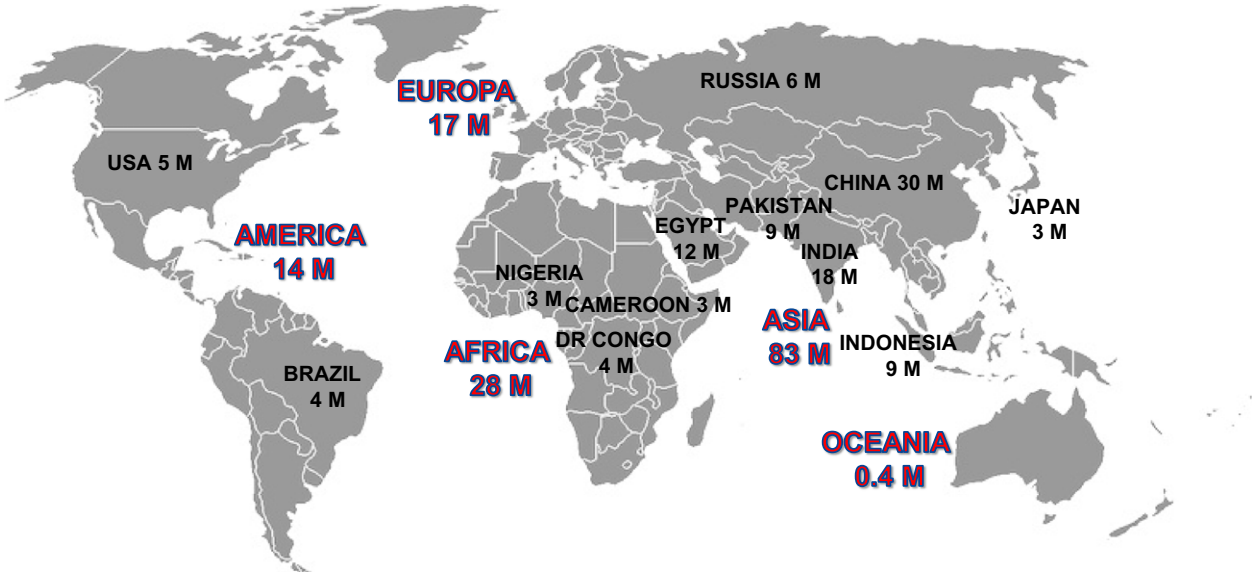


**Fig. 1.** Prevalence of HCV in different countries. The majority of HCV infected people live in Asia and Africa. Several data suggest that the prevalence of HCV is higher in countries located in Asia (2.1%, 83 millions) and Africa (3.2%, 28 millions), while a lower prevalence is found in North America, Europe and Australia (1–3, 20).

**Table 1.** Routine HCV testing is recommended according to different guidelines (CDC and USPSTF; AASLD, WHO)

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| Centre for disease control (CDC) and the USA preventive services task force (USPSTF) |
| Adults born during 1945–1965 should receive one-time testing for HCV without prior ascertainment of HCV risk. |
| Persons who ever injected illegal drugs, including those who injected once or a few times many years ago and do not consider themselves as drug users. |
| Persons with selected medical conditions, including |
| Persons who received clotting factor concentrates produced before 1987; |
| Persons who were ever on chronic (long term) haemodialysis and |
| Persons with persistently abnormal alanine aminotransferase levels. |
| Prior recipients of transfusions or organ transplants, including |
| Persons who were notified that they received blood from a donor who later tested positive for HCV infection; |
| Persons who received a transfusion of blood or blood components before July 1992; and |
| Persons who received an organ transplant before July 1992. |
| Routine HCV testing is recommended for persons with recognized exposures, including |
| Healthcare, emergency medical and public safety workers after needle sticks, sharps or mucosal exposures to HCV-positive blood. |
| Children born to HCV-positive women. |
| American Association for the Study of the Liver (AASLD) |
| HCV testing is recommended at least once for persons born between 1945 and 1965 |
| Other persons should be screened for risk factors for HCV infection, and one-time testing should be performed for all persons with behaviours, exposures and conditions associated with an increased risk of HCV infection |
| Risk behaviours |
| Injection-drug use (current or ever, including those who injected once) |
| Intranasal illicit drug use |
| Risk exposures |
| Long-term haemodialysis (ever) |
| Getting a tattoo in an unregulated setting |
| Healthcare, emergency medical and public safety workers after needle sticks, sharps or mucosal exposures to HCV-infected blood |
| Children born to HCV-infected women |
| Prior recipients of transfusions or organ transplants, including persons who: |
| were notified that they received blood from a donor who later tested positive for HCV infection |
| received a transfusion of blood or blood components, or underwent an organ transplant before July 1992 |
| received clotting factor concentrates produced before 1987 |
| were ever incarcerated |
| Other medical conditions |
| HIV infection |
| Unexplained chronic liver disease and chronic hepatitis including elevated alanine aminotransferase levels |
| World Health Organisation (WHO) |
| Persons who have received medical or dental interventions in healthcare settings where infection control practices are substandard |
| Persons who have received blood transfusions prior to the time when serological testing of blood donors for HCV was initiated or in countries where serological testing of blood donations for HCV is not routinely performed |
| Persons who inject drugs (PWID) |
| Persons who have had tattoos, body piercing or scarification procedures done where infection control practices are substandard |
| Children born to mothers infected with HCV |
| Persons with HIV infection |
| Persons who have used intranasal drugs |
| Prisoners and previously incarcerated persons |

prevalence. According to data from the 2010 USA census, there are approximately 1 74 000 individuals from Egypt currently residing in the USA (12). Recent data from a viral hepatitis community outreach program in New York City, found that 15% of persons born in Egypt residing in the USA are positive for HCV (13). Infected persons from the HONE programme included 30% of persons who did not admit to traditional risk factors for HCV or fall within the birth cohort screening criteria. These patients would have been missed by current screening guidelines. While the HONE study was conducted in one city, it may suggest a broader problem regarding HCV infection in Egyptians in the USA. In France, at Beaujon Hospital, approximately 20% of patients admitted for chronic HCV, are infected with genotype 4 (14). Of these HCV genotype four infected persons, approximately one-third were born in Egypt (15). The majority of these patients grew up in Egypt and came to France when they were adults. The IOM report recently made a recommendation to consider screening persons from Egypt for HCV. Data from both the HONE programme and France support immediate screening of persons for HCV in those originating from Egypt and an appeal

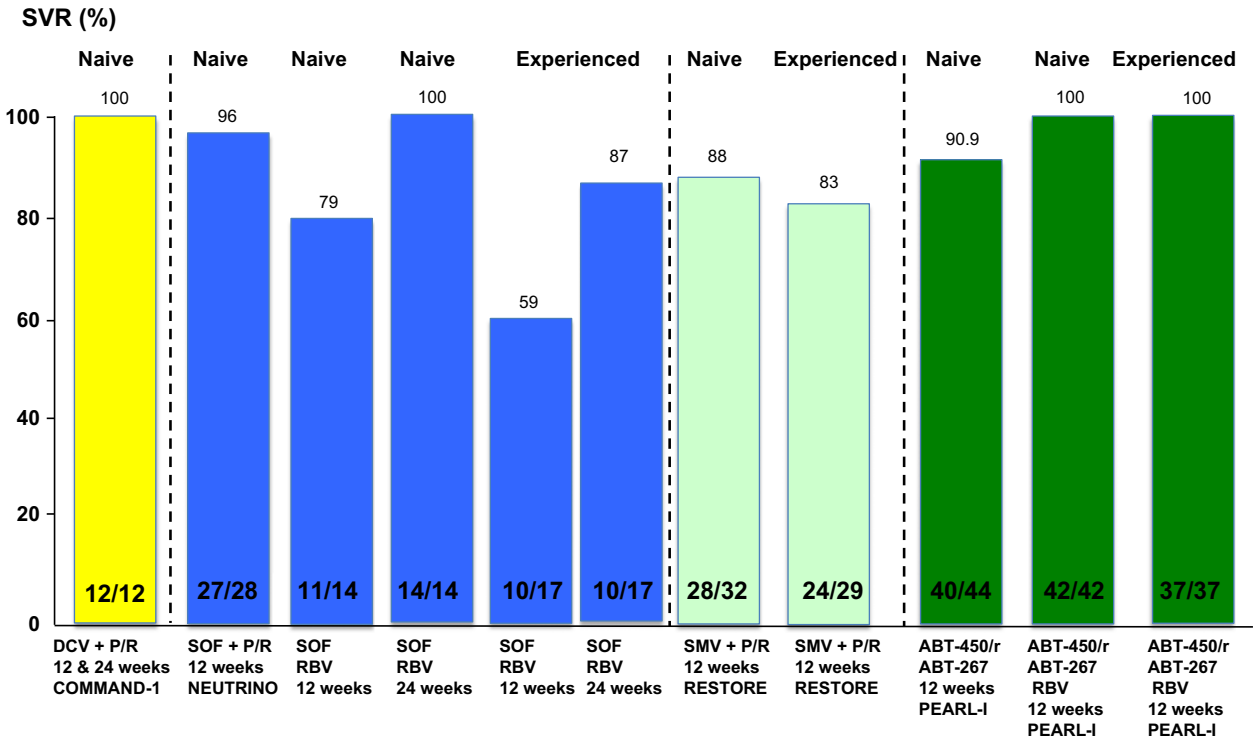


**Fig. 2.** Results of treatment with Direct-acting antivirals (DAAs) for HCV genotype 4 infection [reference (23–27)]. Abbreviations: SOF, sofosbuvir; PR, pegylated interferon/ribavirin; DCV, daclatasvir; SMV, simeprevir.

for additional data regarding prevalence of HCV infection in persons originating from other HCV high prevalence countries.

Worldwide, there is a substantial preventable burden of HCV because of iatrogenic transmission. Transfusion-associated HCV infection is a major worldwide risk before HCV testing became available in 1989. The risk of acquiring HCV via blood transfusion has been virtually eliminated in countries that have implemented routine HCV testing of donors. However, some countries have not prioritized blood transfusion safety and/or lack the resources to implement donor screening, and in these countries blood transfusion remains an important source of infection. There is a high prevalence of transfusions, reuse of needles and syringes, needle-stick injuries among healthcare workers, and unnecessary medication injections (16). It has been estimated that approximately two million HCV infections are acquired annually from contaminated healthcare injections, and may account for up to 40% of all HCV infections worldwide (17). In addition to unsafe injection practices, poor or nonexistent infection control in health and dental care facilities may be a source of HCV transmission in some countries. In Egypt, where the prevalence of HCV is the highest in the world, the reuse of glass syringes during the parenteral therapy campaigns to control endemic schistosomiasis is widely held to be responsible for a very large number of iatrogenic transmissions (18). To be fair, there may have been other concurrent iatrogenic exposures at the time (19). More recent evidence in Egypt supports continuing iatrogenic exposures which contribute to ongoing HCV transmission (19, 20).

Chronic hepatitis B (HBV), unlike HCV, has high vertical transmission rates. Persons born abroad with HBV infection are almost universally infected during birth, thus the population prevalence of HBV in a specific country is a close proxy indicator for the prevalence among individuals who were born in that specific country but who now reside in the USA. Therefore, the CDC and other guidelines have recommended screening for HBV in persons originating from countries with HBsAg prevalence higher than 2% (21,22). Unlike HBV, immigration to the USA reduces the probability of HCV exposure given that the primary route of transmission of HCV in high prevalence countries is iatrogenic. Therefore, specific country prevalence estimates of HCV are likely to overestimate the prevalence of individuals born in that country but now residing in the USA. It is unclear what the best threshold for HCV Ab country prevalence will be necessary to include for identifying additional cases of HCV that would otherwise be missed with current screening practices. We would recommend additional data studies by the CDC and other groups to help determine the country-specific HCV Ab prevalence to use in developing additional guidelines.

There is realistic hope for an oral regimen against HCV in the near future, as several direct-acting antivirals with different mechanisms of action are in advanced drug development (5). For instance, for HCV genotype 4, results of treatment with DAAs are presented in Fig. 2. Some of these drugs or drug combinations have pan-genotypic activity. This rapid progress strongly suggests that IFN-free short duration DAA combinations will make HCV the first chronic viral infection to be eradicated worldwide. The ideal goal will be the eradication of HCV worldwide, and we will have to take into account the significant epidemiological differences changes worldwide.

Finally, we commend the CDC for updating their guidelines for HCV screening. However, there are likely to be at-risk foreign-born persons who originate from HCV high prevalence countries that may still be missed with the current guidelines. To help identify additional cases of HCV, we recommend screening for HCV in persons born in Egypt and Cameroon immediately and investigation of the testing of persons from other countries with high HCV prevalence regions in the future. Of course, we need more research and epidemiological data regarding HCV prevalence worldwide, and to look at HCV among immigrants, in Europe and the USA. With the progress of HCV therapy with oral DAAs, screening will be even more important with the possibility of HCV eradication. With the hope of improving access to therapy, a «test and treat» strategy may become cost-effective and relevant in the future.

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