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WJH covers topics concerning liver biology/pathology, cirrhosis and its complications, liver fibrosis, liver failure, portal hypertension, hepatitis B and C and inflammatory disorders, steatohepatitis and metabolic liver disease, hepatocellular carcinoma, biliary tract disease, autoimmune disease, cholestatic and biliary disease, transplantation, genetics, epidemiology, microbiology, molecular and cell biology, nutrition, geriatric and pediatric hepatology, diagnosis and screening, endoscopy, imaging, and advanced technology. Priority publication will be given to articles concerning diagnosis and treatment of hepatology diseases. The following aspects are covered: Clinical diagnosis, laboratory diagnosis, differential diagnosis, imaging tests, pathological diagnosis, molecular biological diagnosis, immunological diagnosis, genetic diagnosis, functional diagnostics, and physical diagnosis; and comprehensive therapy, drug therapy, surgical therapy, interventional treatment, minimally invasive therapy, and robot-assisted therapy.

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Comparison of hepatitis C virus testing recommendations in high-income countries

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Abstract

AIM

To investigate hepatitis C virus (HCV) testing recommendations from the United States and other high-income countries.

METHODS

A comprehensive search for current HCV testing recommendations from the top quartile of United Nations Human Development Index (HDI) countries (very high HDI) was performed using Google and reviewed from May 1 - October 30, 2014 and re-reviewed April 1 - October 2, 2017.

RESULTS

Of the 51 countries identified, 16 had HCV testing recommendations from a government body or recommendations issued collaboratively between a government and a medical organization. Of these 16 countries, 15 had HCV testing recommendations that were primarily risk-based and highlight behaviors, exposures, and conditions that are associated with HCV transmission in that region. In addition to risk-based testing, the HCV Guidance Panel (United States) incorporates recommendations for a

one-time test for individuals born during 1945-1965 (the birth cohort) without prior ascertainment of risk into their guidance. In addition to the United States, six other countries either have an age-based testing recommendation or recommend one-time testing for all adults independent of risk factors typical of the region.

CONCLUSION

This review affirmed the similarities of the HCV Guidance Panel's guidance with those of recommendations from very high HDI countries.

Key words: Hepatitis C; Testing; Recommendations; Mass screening; Guidelines

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Core tip: This report investigates hepatitis C virus (HCV) testing recommendations from the United States and other high-income countries to assess any risk-based or universal screening categories that should be considered for updates to HCV testing guidance from the HCV Guidance Panel (United States). This review affirmed the similarities of the HCV Panel guidance with those of very high-income countries. No significant gaps in the guidance were identified. HCV testing recommendations from very high-income countries will be continually reviewed and as new risk categories or universal screening recommendations are identified, they will be considered for incorporation into the HCV Panel guidance when peer-reviewed evidence is available to support the incorporation of the HCV testing practices in the United States.

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INTRODUCTION

Hepatitis C virus (HCV) infection, the leading cause of liver cancer and liver failure, is now curable with the recent emergence of short-duration, non-toxic, all-oral therapies^[1-4]. This breakthrough in curative therapies for HCV infection has renewed interest in developing mechanisms to improve the HCV care continuum (testing, linkage to care, treatment initiation, cure). Notably, estimates suggest that 50% of HCV infected individuals remain undiagnosed^[5]. Thus, it has become extremely important in infectious disease public health policy to identify the appropriate groups of individuals to test for HCV infection and to have this information readily available to healthcare professionals.

To provide healthcare professionals with a single web-based resource for evidence-based, expert-devel-

oped recommendations for hepatitis C testing and management, the American Association for the Study of Liver Diseases (AASLD) and the Infectious Diseases Society of America (IDSA) formed the HCV Guidance Panel^[6]. The HCV Guidance Panel is also supported, in part, by the Centers for Disease Control and Prevention (CDC) and the International Antiviral Society United States (IAS-USA). The guidance published by the HCV Guidance Panel (the HCV Panel guidance) are updated periodically as new evidence is reviewed, including any updates to formal recommendations from the CDC and United States Preventive Services Task Force (USPSTF)^[6-8]. In preparation for making updates to the HCV Panel guidance, HCV testing recommendations from the top quartile of United Nations Human Development Index (HDI) countries were evaluated for similarities and differences^[9]. These data have been used periodically by the HCV Guidance Panel to explore HCV testing recommendations globally for comparison to the United States and for consideration in updating the HCV Panel guidance when additional peer-review data is available to support the inclusion of the category in the United States. For example, the periodic reviews of global HCV testing recommendations have served to inform discussion on categories that are not included in the HCV Panel guidance. Any new categories for consideration by panel members are reviewed and literature searches are conducted to ensure that the panel addresses all relevant data on the subject^[6]. Each guidance statement is then rated in terms of the level and strength of evidence^[6].

MATERIALS AND METHODS

The HDI is a summary measure of average achievement in health, education, and gross national income per capita^[9]. Fifty-one countries including the United States were identified as having a very high HDI, defined as the top quartile of HDI countries^[9]. A comprehensive search for current HCV testing recommendations from the top quartile of HDI countries was performed using a Google search with a combination of free text terms. Relevant terms included: country name, hepatitis C, HCV, screening, testing, recommendations, and guidelines. The Google results were then reviewed with experts in the field of hepatitis C (including email and in-person interviews) inquiring about any additional countries known to have HCV testing recommendations.

Testing recommendations were considered if they were from a government body or represented collaborative recommendations between a government and a medical organization. To be included in our analysis, recommendations needed to be available online May 1, 2014 - October 2, 2017. Non-English language documents were translated into English using Google Translate. When logical, testing categories were combined to make the tabulation of the results more manageable. Because in the United States both the CDC and USPSTF independently issue HCV testing recommendations, the HCV Guidance Panel's routine synthesis of these recom-

recommendations into their guidance were used for the purpose of this report. From May 1 - October 30, 2014, two reviewers performed the initial searches and engaged consultants to identify HCV testing recommendations from very high HDI countries. Two reviewers re-reviewed HCV testing recommendations through Google searches and follow up with expert consults from April 1 - October 2, 2017 to identify and update any changes.

RESULTS

Of the 51 countries categorized as very high HDI, 16, including the United States were found to have HCV testing recommendations (Table 1)^[6,10-26]. Of these 16 countries, 15 had HCV testing recommendations that were primarily risk-based and highlight behaviors, exposures, and conditions that are associated with HCV transmission in that region. In addition to risk-based testing, the HCV Panel guidance incorporates CDC and USPSTF recommendations for a one-time test for individuals born during 1945-1965 (the birth cohort) without prior ascertainment of risk^[6-8]. Six additional countries have either an age-based testing recommendation or recommend one-time testing for all adults independent of risk factors. In the United States, individuals born from 1945-1965 are included in both CDC and USPSTF HCV testing recommendations as they account for 75% of all HCV infections and evidence confirmed that a risk-based strategy alone failed to identify more than 50% of HCV infections due to provider and patient barriers in correctly ascertaining risk^[6,27].

The HCV Panel guidance recommends one-time testing for all HIV-positive individuals and for any persons about to start pre-exposure prophylaxis (PrEP) for HIV. The HCV Panel guidance also recommends annual HCV testing for persons who inject drugs and for HIV-infected men who have unprotected sex with men.

As of 2017, the HCV testing categories identified in other very high HDI countries not included in the HCV Panel guidance are: (1) Acute hepatitis or hepatitis symptoms; (2) Receiving an immunization or a medical procedure in a specified country or in a country where hepatitis C is common or where universal precautions are not in place; (3) Body piercing or tattoo history; (4) Hemophilia history; (5) Hepatitis A or B infection history; (6) Homeless persons; (7) Immigrants or visitors from countries where HCV is endemic; (8) Liver Cancer; (9) Living with, or sexual partner of, HCV-positive person; (10) Multiple sex partners, history of sexually transmitted infections (STIs), or high risk sexual behaviors; and (11) Attending STI clinic (\pm any risk factors)

DISCUSSION

The HCV Panel guidance is based on epidemiologic data and behaviors, exposures, and conditions associated with acquisition of HCV infection in the United States and are compiled by the expert panel and reviewed regularly^[6]. As a result of this initial work in 2014, solid organ donors

(deceased and living) were identified as a group not included in the guidance and were thus considered for review. After additional review of the available literature on the subject, donors were added to the HCV Panel guidance in 2014 and given an evidence rating of Class I, Level B^[6,28,29]. Prior to this, donors had not been explicitly named as a testing category but were discussed in the text below the testing guidance.

Currently, the HCV Panel guidance include the vast majority of HCV testing recommendation categories noted in other HDI countries and many of the people within risk categories not directly specified would likely receive testing nonetheless because of other associated risks or because of typical clinical care in the United States. For instance, acute hepatitis/hepatitis symptoms, hepatitis A or B history, and liver cancer would prompt a clinical evaluation for hepatitis C and might also be captured by the HCV Guidance Panel category of unexplained chronic liver disease and/or chronic hepatitis including elevated alanine aminotransferase levels^[6]. Additionally, hemophilia alone is not recommended for testing by the HCV Guidance Panel; however, certain persons with hemophilia would be tested for HCV because the HCV Panel guidance incorporates recommendations to screen anyone who received blood components before 1992 or clotting factor concentrates produced before 1987 for HCV^[6]. The remaining recommendation categories covered by other very high HDI countries but not included in the HCV Panel guidance include: body piercing or tattoo history; being homeless; living with, or the sexual partner of, an HCV-positive person; multiple sex partners, history of STIs, or high risk sexual behaviors; STI clinic populations; and immigrants/visitors from countries where HCV is endemic or those vaccinated or receiving medical procedures in those countries or where universal precautions are not in place. Although body piercings and tattoos are not specifically mentioned in the HCV Panel guidance, they do incorporate recommendations to test persons with percutaneous/parenteral exposures in an unregulated setting^[6]. Hence, according to the HCV Guidance Panel, individuals with body piercings/tattoos obtained outside of licensed parlors should undergo HCV testing. Furthermore, this practice would also likely capture medical procedures where strict infection control may not have been followed, both domestically and internationally. While the higher prevalence of HCV in homeless populations is acknowledged by the HCV Guidance Panel, the homeless are not specifically named as a group for testing at this time. Although several studies have noted prevalence rates above 10% in several homeless populations in the United States, it is believed that the risk is often due to high rates of substance use disorders, which would be captured by the HCV Panel guidance to test injection and intranasal drug users^[30]. Sexual transmission of HCV is generally considered inefficient except among HIV-infected MSM; therefore, guidance related to sexual transmission categories for the general United States population have not been included as an HCV testing

Table 1 Hepatitis C virus testing recommendations from the top quartile of human development index countries

Countries and approving bodies	Yr Recommendations approved	Abnormal Aminotransferases	Acute hepatitis or hepatitis symptoms	Being immunized/receiving a medical procedure in a specified country where hepatitis C is common or lack of universal precautions	Birth cohort/age recommendations or one-time testing for all	Blood/clotting factor transfusion Patients/ Transplant Patients	Body Piercing or Tattoo History	Children born to HCV-infected mothers (expectant mothers)
Argentina	2016	X	X	X	X	X		X
Dirección de Sida y ETS, Ministerio de Salud de la Nación								
Australia	2016	X	X			X	X	X
National HCV Testing Policy Expert Reference Committee								
Canada	2017 and 2009	X	X	X		X	X	X
Canadian Task Force on Preventive Health Care								
Chile	2015	X			X	X		X
Ministerio de Salud de Chile (Chilean Ministry of Health)								
Denmark	2013	X				X		X
Sundhedsstyrelsen (Danish Health Authority)								
Finland	2016			X	X	X	X	X
Sosiaalija terveysministeriö (Social and Health Ministry)								
France	2014	X		X	X	X	X	X
ANRS/AFEF with Ministère des Affaires sociales et de la Santé (Ministry of Social Affairs and Health)								
Greece	2017	X			X	X		X
Υπουργείο Υγείας (Ministry of Health)								
Ireland	2012	X		X		X	X	X
Feidhmeannacht na Seirbhíse Slainte								
Italy	2005					X		
Istituto Superiore di Sanità								
Japan	2011				X			
Ministry of Health, Labour and Welfare								
Russian Federation	2017		X			X		X
Министерство здравоохранения (Ministry of Health)								
Spain	2015					X	X	X
Ministerio de Sanidad, Servicios Sociales e Igualdad (Ministry of Health, Social Services and Equality)								
Switzerland	2013	X	X	X		X	X	X
Bundesamt für Gesundheit (Swiss Federal Office of Public Health)								
United Kingdom	2015 and 2012	X		X		X	X	X
NHS and National Inst for Health and Care Excellence								
United States	2017	X			X	X		X
HCV Guidance Panel								

HCV: Hepatitis C virus; MSM: Men who have sex with men; X denotes that category is advised for testing.

Table 1 Hepatitis C virus testing recommendations from the top quartile of human development index countries

Countries and approving bodies	Chronic liver disease, cirrhosis, or fibrosis	Contact tracing /exposure to infected person	Donors - blood, blood product, tissue or organ	Drug users - injecting	BDrug users - intranasal	Healthcare workers (public safety) at risk and/or post-exposure	Hemodialysis history or repeated percutaneous injections	Hemophilia history	Hepatitis A or B history (or non-A/non-B hepatitis)
Argentina				X	X		X		X
Dirección de Sida y ETS, Ministerio de Salud de la Nación									
Australia	X	X	X	X		X	X		X
National HCV Testing Policy Expert Reference Committee									
Canada	X	X		X	X		X	X	X
Canadian Task Force on Preventive Health Care									
Chile	X			X		X	X	X	
Ministerio de Salud de Chile (Chilean Ministry of Health)									
Denmark	X			X	X	X	X	X	X
Sundhedsstyrelsen (Danish Health Authority)									
Finland			X	X	X				
Sosiaali- ja terveysministeriö (Social and Health Ministry)									
France		X	X	X	X		X		
ANRS/AFFEF with Ministère des Affaires sociales et de la Santé (Ministry of Social Affairs and Health)									
Greece				X			X		X
Υπουργείο Υγείας (Ministry of Health)									
Ireland			X	X	X	X	X		X
Feidhmeannacht na Seirbhíse Slainte									
Italy				X			X		
Istituto Superiore di Sanità									
Japan									
Ministry of Health, Labour and Welfare									
Russian Federation	X	X	X	X		X	X		X
Министерство здравоохранения (Ministry of Health)									
Spain		X		X	X	X	X		X
Ministerio de Sanidad, Servicios Sociales e Igualdad (Ministry of Health, Social Services and Equality)									
Switzerland	X			X	X	X	X		X
Bundesamt für Gesundheit (Swiss Federal Office of Public Health)									
United Kingdom				X					
NHS and National Inst for Health and Care Excellence									
United States	X	X	X	X	X	X	X		
HCV Guidance Panel									

MSM: Men who have sex with men; X denotes that category is advised for testing.

Table 1 Hepatitis C virus testing recommendations from the top quartile of human development index countries

Countries and approving bodies	HIV-positive patients	Homeless	Immigrants or visitors from countries where HCV is endemic	Incarceration history alone or with additional risk factors	Liver cancer	Living with or sexual partner of HCV-positive person	MSM, limited to HIV + MSM (with or without unprotected sex), or sexually active starting PrEP	Multiple Sex Partners, history of STIs, or high risk sexual behaviors	Patient request, percutaneous- parenteral exposure, prior positive HCV test	STI clinic (+/- any risk factors)
Argentina						X		X	X	
Dirección de Sida y ETS, Ministerio de Salud de la Nación										
Australia	X		X	X	X	X	X		X	X
National HCV Testing Policy Expert Reference Committee										
Canada	X	X	X	X				X	X	
Canadian Task Force on Preventive Health Care										
Chile	X				X	X				
Ministerio de Salud de Chile (Chilean Ministry of Health)										
Denmark	X		X		X					
Sundhedsstyrelsen (Danish Health Authority)										
Finland	X		X	X			X	X		
Sosiaali- ja terveysministeriö (Social and Health Ministry)										
France	X		X	X		X	X			
ANRS/AFEF with Ministère des Affaires sociales et de la Santé (Ministry of Social Affairs and Health)										
Greece	X		X	X		X		X	X	
Υπουργείο Υγείας (Ministry of Health)										
Ireland	X		X	X		X	X		X	
Feidhmeannacht na Seirbhíse Slainte										
Italy						X		X	X	
Istituto Superiore di Sanità										
Japan										
Ministry of Health, Labour and Welfare										
Russian Federation				X		X	X	X		
Министерство здравоохранения (Ministry of Health)										
Spain	X			X		X	X		X	
Ministerio de Sanidad, Servicios Sociales e Igualdad (Ministry of Health, Social Services and Equality)										
Switzerland	X		X	X	X	X	X		X	
Bundesamt für Gesundheit (Swiss Federal Office of Public Health)										
United Kingdom		X	X	X		X	X		X	X
NHS and National Inst for Health and Care Excellence										
United States	X			X			X		X	
HCV Guidance Panel										

HIV: Human immunodeficiency virus; HCV: Hepatitis C virus; STI: Sexually transmitted infection; MSM: Men who have sex with men; X denotes that category is advised for testing.

category^[31]. STI clinics are also not currently included in the HCV Panel guidance. Data suggest that STI clinic populations have higher prevalence rates of HCV infection than the general population due to overlapping risk factors of sexually transmitted infections and hepatitis C^[32,33]. However, the higher prevalence of HCV infection in STI clinic populations is often attributed to the birth cohort (individuals born between 1945 and 1965) and injection drug use, risk groups captured elsewhere in the guidance^[32-35]. Finally, while the HCV Guidance Panel continues to review evidence on immigrants/visitors from countries where HCV is endemic, any future guidance for HCV testing among foreign-born individuals would need to account for geographic disparities in HCV prevalence and practicalities in implementing this in clinical practice settings^[36,37]. As an example of how this might be implemented, in 2008 the CDC recommended hepatitis B screening for persons born in regions of high and intermediate HBV endemicity (HBsAg prevalence > 2%)^[38].

Our report has the following limitations. Our search methodology may have missed recommendations and/or classified recommendations incorrectly from some very high HDI countries due to search terms not capturing relevant information in different languages, recommendations not being accessible on the Internet at the time of the searches, or misinterpretation of the role of the government's involvement in development of the recommendations. Additionally, some governments may rely on international or national organizations for recommendations on hepatitis C testing without publishing their own recommendations.

This review affirmed the similarities of the HCV Panel guidance with those of very high HDI countries. No significant gaps in the guidance were identified. HCV testing recommendations from very high HDI countries will be continually reviewed and as new risk categories or universal screening recommendations are identified, they will be considered for incorporation into the HCV Panel guidance when peer-reviewed evidence is available to support the incorporation of the HCV testing practices in the United States.

ARTICLE HIGHLIGHTS

Research background

Hepatitis C virus (HCV) infection, the leading cause of liver cancer and liver failure, is now curable with the recent emergence of short-duration, non-toxic, all-oral therapies. This breakthrough in curative therapies for HCV infection has renewed interest in developing mechanisms to improve the HCV care continuum (testing, linkage to care, treatment initiation, cure). This renewed interest in HCV has led to many countries updating their HCV testing recommendations.

Research motivation

The United States HCV Guidance Panel provides healthcare professionals with a single web-based resource for evidence-based, expert-developed recommendations for hepatitis C testing and management. HCV recommendations in countries around the world have been recently updated due to advances in HCV treatment. However, this data is not compiled in a central location. This report investigates HCV testing recommendations from the United

States and other high-income countries. In preparation for making updates to the HCV Panel guidance, HCV testing recommendations from the top quartile of United Nations Human Development Index (HDI) countries were evaluated for similarities and differences.

Research objectives

The main objective of this study was to identify HCV testing recommendations from the top quartile of United Nations HDI countries. The identified HCV recommendations were evaluated for similarities and differences. These data have been used periodically by the HCV Guidance Panel to explore HCV testing recommendations globally for comparison to the United States for consideration in updating the HCV Panel guidance when additional peer-review data is available to support inclusion of the category in the United States.

Research methods

A comprehensive search for current HCV testing recommendations from the top quartile of HDI countries was performed using a Google search with a combination of free text terms. Relevant terms included: country name, hepatitis C, HCV, screening, testing, recommendations, and guidelines. The Google results were then reviewed with experts in the field of hepatitis C (including email and in-person interviews) inquiring about any additional countries known to have HCV testing recommendations. Testing recommendations were considered if they were from a government body or represented collaborative recommendations between a government and a medical organization. To be included in our analysis, recommendations needed to be available online May 1, 2014–October 2, 2017. From May 1–October 30, 2014, two reviewers performed the initial searches and engaged consultants to identify HCV testing recommendations from very high HDI countries. Two reviewers re-reviewed HCV testing recommendations through Google searches and follow up with expert consults from April 1–October 2, 2017 to identify and update any changes.

Research results

Of the 51 countries identified, 16 had HCV testing recommendations from a government body or recommendations issued collaboratively between a government and a medical organization. Of these 16 countries, 15 had HCV testing recommendations that were primarily risk-based and highlight behaviors, exposures, and conditions that are associated with HCV transmission in that region. In addition to risk-based testing, the HCV Guidance Panel (United States) incorporates recommendations for a one-time test for individuals born during 1945–1965 (the birth cohort) without prior ascertainment of risk into their guidance. In addition to the United States, six other countries either have an age-based testing recommendation or recommend one-time testing for all adults independent of risk factors typical of the region.

Research conclusions

This review affirmed the similarities of the HCV Guidance Panel's guidance with those of recommendations from very high HDI countries. As a result of this initial work in 2014, solid organ donors (deceased and living) were identified as a group not included in the guidance and were thus considered for review. After additional review of the available literature on the subject, donors were added to the HCV Panel guidance in 2014 and given an evidence of rating of Class I, Level B. Prior to this, donors had not been explicitly named as a testing category but were discussed in the text below the testing guidance.

Research perspectives

HCV testing recommendations from very high HDI countries will be continually reviewed and as new risk categories or universal screening recommendations are identified, they will be considered for incorporation into the HCV Panel guidance when peer-reviewed evidence is available to support the incorporation of the HCV testing practices in the United States.

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