

Accepted Manuscript

Special report

Report from a Viral Hepatitis Policy Forum on Implementing the WHO Framework for Global Action on Viral Hepatitis in North Asia

Ding-Shinn Chen, Stephen Locarnini, Suzanne Wait, Si-Hyun Bae, Pei-Jer Chen, James YY Fung, Hong Soo Kim, Sheng-Nan Lu, Joseph Sung, Junko Tanaka, Takaji Wakita, John Ward, Jack Wallace and the CEVHAP North Asia Workshop on Viral Hepatitis

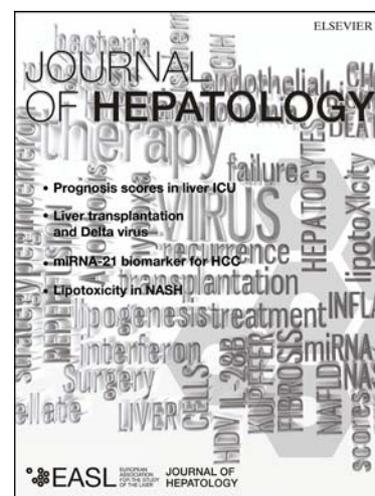
PII: S0168-8278(13)00447-9
DOI: <http://dx.doi.org/10.1016/j.jhep.2013.06.029>
Reference: JHEPAT 4783

To appear in: *Journal of Hepatology*

Received Date: 4 April 2013
Accepted Date: 29 June 2013

Please cite this article as: Chen, D-S., Locarnini, S., Wait, S., Bae, S-H., Chen, P-J., Fung, J.Y., Kim, H.S., Lu, S-N., Sung, J., Tanaka, J., Wakita, T., Ward, J., Wallace, J., and the CEVHAP North Asia Workshop on Viral Hepatitis Report from a Viral Hepatitis Policy Forum on Implementing the WHO Framework for Global Action on Viral Hepatitis in North Asia, *Journal of Hepatology* (2013), doi: <http://dx.doi.org/10.1016/j.jhep.2013.06.029>

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.



**Report from a Viral Hepatitis Policy Forum on Implementing the WHO
Framework for Global Action on Viral Hepatitis in North Asia**

Ding-Shinn Chen¹, Stephen Locarnini^{2,14}, Suzanne Wait³, Si-Hyun Bae⁴, Pei-Jer Chen⁵, James YY Fung⁶, Hong Soo Kim⁷, Sheng-Nan Lu⁸, Joseph Sung⁹, Junko Tanaka¹⁰, Takaji Wakita¹¹, John Ward¹², Jack Wallace¹³ and the CEVHAP North Asia Workshop on Viral Hepatitis*

*Participants of the Coalition to Eradicate Viral Hepatitis in Asia Pacific [CEVHAP] North Asia Workshop on Viral Hepatitis included: from Taiwan: Ding-Shinn Chen, Pei-Jer Chen, Sheng-Nan Lu, Pei-Ming Yang; from Hong Kong: Joseph Sung, Ching-Lung Lai, James YY Fung; from Korea: Si Hyun Bae, June Sung Lee, Hong Soo Kim, Sang-Hoon Ahn, Goo Hyeon Yoon; from Japan: Junko Tanaka, Takaji Wakita, Hideki Aizaki, Atsuko Yonezawa, Yukio Lino, Yoichi Abe; from the United States: John Ward, Lily Lou; from the UK: Charles Gore; from Malaysia: Rosmawati Mohamed; from Australia: Stephen Locarnini and Jack Wallace. The workshop was facilitated by Suzanne Wait [UK] and Jennifer Johnston [Australia].

Author affiliations:

1. National Taiwan University College of Medicine, Taipei, Taiwan
2. Molecular Research, Victorian Infectious Diseases Reference Laboratory, North Melbourne, Australia
3. SHW Health Limited, London, United Kingdom
4. Department of Internal Medicine, Seoul St. Mary Hospital, Catholic University Medical College, Seoul, Korea

5. Hepatitis Research Centre, National Taiwan University and Hospital, Taipei, Taiwan
6. Department of Medicine, The University of Hong Kong, Queen Mary Hospital, Hong Kong
7. Division of Gastroenterology, Department of Internal Medicine, SoonChunHyang University Hospital, Cheonan, Korea
8. Division of Hepatogastroenterology, Department of Internal Medicine, Kaohsiung Chang Gung Memorial Hospital, Kaohsiung, Taiwan
9. The Chinese University of Hong Kong, Shatin, Hong Kong
10. Department of Epidemiology Infectious Disease Control and Prevention, Hiroshima University Institute of Biomedical and Health Sciences. Hiroshima, Japan
11. Department of Virology II, National Institute of Infectious Diseases, Tokyo, Japan
12. Division of Viral Hepatitis, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, Centers for Disease Control and Prevention Atlanta, Georgia, United States
13. Australian Research Center in Sex, Health and Society, LaTrobe University, Melbourne, Australia
14. To whom all correspondence should be addressed

Corresponding Author:

Professor Stephen Locarnini

Head, Research & Molecular Development

Victorian Infectious Diseases Reference Laboratory

Director, WHO Regional Reference Laboratory for Hepatitis B

10 Wreckyn Street, North Melbourne, VIC, 3051 Australia

Ph: 61-3-9342 2637

Fax: 61-3-9342 2666

Email: Stephen.Locarnini@mh.org.au

Electronic word count: 3725

Conflicts of interest: None

Financial support:

The CEVHAP North Asia Forum was made possible through unrestricted grants and core funding from Bristol-Myers Squibb, Merck, Gilead and Janssen. This publication was funded by CEVHAP as part of this workshop.

Abstract

Background and aims: The World Health Organisation [WHO] Prevention & Control of Viral Hepatitis Infection: Framework for Global Action offers a global vision for the prevention and control of viral hepatitis. In October 2012, the Coalition to Eradicate Viral Hepatitis in Asia Pacific [CEVHAP] organised the North Asia Workshop on Viral Hepatitis in Taipei to discuss how to implement the WHO Framework in the North Asia region. This paper presents outcomes from this workshop.

Methods: Twenty-eight representatives from local liver associations, patient organisations and centres of excellence in Hong Kong, Japan, Korea and Taiwan participated in the workshop.

Findings: Priority areas for action were described along the four axes of the WHO Framework: 1. Awareness, advocacy and resources; 2. Evidence and data; 3. Prevention of transmission; and 4. Screening and treatment. Priorities included: Axis 1: Greater public and professional awareness, particularly among primary care physicians and local advocacy networks. Axis 2: Better economic data and identifying barriers to screening and treatment uptake. Axis 3: Monitoring of vaccination outcomes and targeted harm reduction strategies. Axis 4: Strengthening links between hospitals and primary care providers, and secure funding of screening and treatment, including for hepatocellular carcinoma.

Conclusions: The WHO Framework provides an opportunity to develop comprehensive and cohesive policies in North Asia and the broader region. A partnership between clinical specialists, primary care physicians, policy makers, and people with or at risk of viral hepatitis is essential in shaping future policies.

Key words: hepatitis B, hepatitis C, Asia, policy.

1. Introduction

In 2012, the World Health Organisation [WHO] launched the ***Prevention & Control of Viral Hepatitis Infection: Framework for Global Action***. This strategy offers a global vision for the prevention and control of viral hepatitis. [1] The Framework was welcomed by hepatitis experts and advocacy groups who have been struggling for the attention of policymakers about this 'silent epidemic' for many years. [2, 3]

Asia is home to 75% of all chronic hepatitis B cases [4] and China alone has more cases of hepatitis C infection than all of Europe or the Americas.[5] The majority of people infected with either hepatitis B virus or hepatitis C virus do not know that they are infected, and are not aware of the precautions they need to take to avoid infecting others or to enable them to reduce the impact of the infection.[6] Uptake of screening, when available, is low, and treatment rates are 4-10% in Asia compared to rates of 20% in the United States.[7]

Against this background, the Coalition to Eradicate Viral Hepatitis in Asia Pacific (CEVHAP) was established in 2010 to contribute towards an Asia Pacific region free from the significant health, social and economic burden of viral hepatitis (www.cevhap.com). CEVHAP is uniquely positioned to support and facilitate the implementation of the WHO framework in different countries across the region through its network of members who are experts in their respective fields in the Asia Pacific region and globally.

In October 2012, CEVHAP organised the North Asia Workshop on Viral Hepatitis in Taipei, with participants from Hong Kong, Japan, Korea and Taiwan. These four jurisdictions were chosen because, to varying degrees, they have some initiatives in place in the area of viral hepatitis and have broadly similar health infrastructures. These localities are also in a privileged position compared to other countries in Asia Pacific region, in that they have the resources to build on existing successes and lead the drive for further policy change across the region. Summary epidemiological data on hepatitis B and hepatitis C in these four jurisdictions is presented in **Table 1**.

The aim of the workshop was to ensure that participants understood the WHO framework; to support participants in building or strengthening advocacy networks, and to identify local priorities for implementing the framework within their respective jurisdictions.

This paper summarises the outcomes of this workshop and identifies steps to be taken to translate the WHO Framework into sustainable national policies on viral hepatitis in North Asia.

2. Materials and methods

The 28 workshop participants were identified within the existing CEVHAP network of local liver associations, patient organisations and centres of excellence in Hong Kong, Japan, Korea and Taiwan. The agenda for the one and a half day workshop was developed in close consultation with a small group of CEVHAP experts. To assist participants in their preparation, a briefing paper describing the scope of viral

hepatitis, focusing on hepatitis C and hepatitis C virus, within the four jurisdictions was distributed prior to the meeting. [CEVHAP, data on file]

The workshop used the four axes of the WHO Prevention & Control of Viral Hepatitis Infection: Framework for Global Action to guide discussions (**Fig. 1**) and consisted of expert presentations, group discussions and country-level workshops.

3. Results

This paper uses the four axes of the WHO framework to describe the workshop results. The priority areas for action in the four participating jurisdictions are presented in **Table 2** and are discussed in more detail in the section below.

Axis 1: Raising awareness, promoting partnerships and securing resources

In North Asia, the general public, people at risk of infection, the medical community and policymakers generally have a poor understanding of viral hepatitis, its natural history and manifestations. Awareness among primary care physicians is particularly low and targeted educational efforts are needed to encourage these providers to test their patients for viral hepatitis and refer them towards appropriate care pathways. Investment in developing better relationships between primary care and hepatitis specialist services may help engage primary care physicians.

Local advocacy networks that bridge civil society, liver specialists, primary care physicians and other community care providers are still lacking in Taiwan, Hong Kong and Korea particularly. This lack of a strong advocacy base makes it more difficult to engage the media in the first place or to overcome media fatigue about viral hepatitis. The media plays a vital role in raising awareness of viral hepatitis, particularly among the general public and those at risk of infection. The awareness campaigns run in the United States and Korea provide interesting examples of media engagement on viral hepatitis (**Case studies 1 and 2**).

A key to the success of awareness campaigns on viral hepatitis is to find the issues that resonate best with media, the public and policymakers. The fact that viral hepatitis is one of the main causes of liver cancer is indeed compelling and one with potential to grab the attention of these key stakeholders. For example, a recent study

by the International Agency for Research on Cancer showed that one in six cancers was caused by infection and concluded that prevention of viral hepatitis and other infections could have a substantial effect on reducing the future burden of cancer.[8] These data may be very powerful in convincing policymakers of the need to mobilise resources towards the prevention and management of viral hepatitis.

Case study 1: How to engage the public on hepatitis: the ‘KNOW More Hepatitis’ in the United States

In 2011, the United States Centers for Disease Control and Prevention (CDC) launched an education campaign, ‘KNOW More Hepatitis’.[9] Insights from focus groups consisting of people with high prevalence rates of infection [for example, ‘baby-boomers’ for hepatitis C] helped guide the development of targeted messages for each risk population.[10] The campaign made creative use of social and other media:

It used powerful, evidence-based messages to engage the media. One example was “Hepatitis now kills more Americans than HIV”, which was the key conclusion of a recently published article in the *Annals of Internal Medicine*. [11]

An online hepatitis risk assessment tool was featured on the CDC website, which allowed individuals to conduct a quick, confidential assessment of their risk for hepatitis A, hepatitis B or hepatitis C in the privacy of their own homes.

The campaign has an active Facebook page, 11,000 followers on Twitter, and public service advertisements on YouTube. 400 tweets translated into over 3.3 million media impressions, demonstrating the power of social media to engage target audiences on viral hepatitis.

Six national airports donated space worth up to \$4 million for Dioramas which featured rotating posters on viral hepatitis (Fig. 2).

ACCEPTED MANUSCRIPT

Case study 2: Conveying the 'right level of fear'? The Korean experience

In March 2011, the Korean Association for the Study of the Liver (KASL) launched an awareness campaign on viral hepatitis. A 30-minute television advertisement showed patients with end-stage liver disease. The message was: "if you don't manage your disease, this is what is going to happen." The goal was to shock the public into action.

The impact of the advertisement was significant: the day after it featured, KASL was ranked top of Google searches. But the increased attention also had unintended adverse consequences: people infected with viral hepatitis reported the loss of relationships or employment as a result of the advertisement. KASL immediately launched a lower-intensity campaign that focused on the importance of seeking proper care for chronic hepatitis infection.

The lesson learned by KASL was that it is important to convey the 'right' level of fear about viral hepatitis in order to raise awareness of the urgency of the situation in terms of the risks of advanced liver disease. However, too much fear may create panic and inertia, if the perceived message is that nothing that can be done to improve the outcomes of people with the viral hepatitis or that policy makers, physicians and the public are powerless to effect change.

Axis 2: Evidence-based policy and data for action

One key condition for successful advocacy and a sustained public health response is reliable data. With viral hepatitis, the fact that so many people remain undiagnosed makes it difficult to convey to policy makers the full scale of the problem. [12] Better surveillance is needed to capture chronic as well as acute cases of viral hepatitis.

More reliable prevalence estimates in high risk populations, such as people who are poor, those who inject drugs, prisoners, and sex workers are needed as these groups are usually poorly represented in existing surveillance studies.

Reliable economic data are critical to demonstrate to national governments the need for them to invest in viral hepatitis prevention and control. Sometimes showing policy makers the cost of 'doing nothing' can exemplify the most compelling case for investment.[13]

One area where more research is greatly needed is to find the barriers to uptake of screening and treatment among individuals at risk. These data are critical to shift the behaviours of individuals towards more active disease management.

Finally, insights from patients, such as those gathered in a survey of the Japan Hepatitis Council (**Case study 3**) may help channel efforts towards areas that will make the greatest difference to individuals living with viral hepatitis.

Case study 3: The combined power of advocacy and data: The Japan Hepatitis Council

Japan has a powerful patient advocacy base consisting of over 80 local, regional and national associations acting under the umbrella of the Japan Hepatitis Council. Pressure from these groups over the government's failure to implement blood and mass vaccination safety measures was instrumental in the creation of the Basic Act of Hepatitis Measures in 2010. As part of this Act, each prefecture is required to have a hepatitis patient representative on its local council.

A recent survey of members of the Japan Hepatitis Council helped identify some of the main challenges for policy development in Japan[14]:

High mortality from hepatocellular carcinoma (HCC): Japan has one of the highest rates of HCC in the world and counts 30,000 deaths due to HCC every year.

Low uptake of screening: A national screening programme against hepatitis B and C has existed since 2002, targeting individuals aged 40-70 years. However, uptake rates remain low (7-27%) and screening is poorly integrated into general practice.[15, 16]

Poor linkage to treatment: 48% of those who test positive for hepatitis B (and 65% of those testing positive for HCV) fail to seek medical care [12] and only half of those with hepatitis C who do seek care complete their course of treatment.[14]

High costs of care: Government funding for antiviral treatment of hepatitis B and hepatitis C has gradually increased since 2008, however patients are still left with a significant co-payment and many patients report crippling personal economic costs.

Stigma and discrimination: Thirty percent of respondents report having experienced discrimination due to viral hepatitis, especially in medical institutions. Several respondents felt that their hepatitis status hindered their marriage prospects and employment options. Many admitted that they hid their condition from others as a result.

Axis 3: Prevention of transmission

Vaccination against hepatitis B has had a marked impact on reducing the incidence of hepatitis B infection (**Case study 4**). However, gaps in the region remain. Japan only offers vaccination to infants born to hepatitis B-infected mothers, whereas in Taiwan this is one group in whom vaccination efforts have been less successful. In all countries, careful evaluation of the impact of vaccination and of the benefits of extending vaccination to high risk groups is needed.

Injecting drug use is now the predominant route of transmission for hepatitis C in north Asia [17] and this is a critical target group for prevention strategies. Co-infection of hepatitis B and hepatitis C and /or HIV is a key concern in people who inject drugs, as it is associated with more rapid progression to liver disease and death.[18, 19] Targeted education and prevention measures, including vaccination, are needed to control transmission in other individuals at high risk of infection, including people who have tattoos and acupuncture, women of childbearing age, men who have sex with men, and prisoners. And continued education about the risks of transmission through sexual contact and the need for safe sex practices is needed for the general population.

Re-use of needles and syringes in medical practice is common practice in Asia and nosocomial spread of hepatitis C has been observed in outpatient clinics [20] as well as dialysis units.[21-23] Information about safe injection practices and the prevention of transmission should be essential components of professional education efforts.

Case study 4: Taiwan: a vaccination success story

Taiwan launched one of the first universal vaccination programmes against hepatitis B in 1984 and the programme is heralded around the world as a true success story.[24, 25] Today, systematic vaccination is offered to all newborns, health workers and schoolchildren who missed the neonatal vaccination [catch up vaccination]. The impact of the programme on seroprevalence levels has been considerable (**Fig. 3**) and horizontal transmission amongst children decreased [26]. The HCC incidence among children has been considerably reduced, making the hepatitis B vaccine the first effective vaccine for the prevention of cancer.[27] The programme has also provided important insights into the natural history of hepatitis B, for example about the duration of conferred immunogenicity and the need for booster vaccinations.[28]

Complacency must be avoided, however, as thousands of deaths due to viral hepatitis still occur every year in Taiwan. Prevalence rates have not decreased in adults [29] and the impact of vaccination is much lower in rural areas than in urban centres.[28, 30] Also, the success of vaccination cannot be taken for granted: diligent, continuous monitoring of the quality of available vaccines and of the outcomes of vaccination programmes is needed for the public health impact of the vaccination programme against hepatitis B virus to continue in Taiwan.[31, 32]

Axis 4: Screening, care and treatment

Greater availability, awareness and uptake of screening for both hepatitis B and hepatitis C were highlighted as the most pressing needs by participants from all countries in the CEVHAP workshop. Countries differ in what screening programmes

have been implemented and to what extent screening is covered by public funds. Barriers to screening are likely to be specific to each local context, not to mention each individual (**Table 3**). It is critical that the confidentiality of screening results is ensured; in many countries, the results of screening may be sent to a person's employer, causing discrimination and often loss of employment for the person concerned.

Another significant issue is the need to ensure greater linkage from screening to treatment, given a large proportion of individuals who test positive at screening are known not to seek treatment. Comprehensive care models are urgently needed to make sure that individuals who are infected receive appropriate information, counselling and care throughout all phases of their condition.[33] In many countries, better collaboration between primary care physicians and liver specialists is needed to ensure that individuals who test positive are referred to appropriate care.

A commonly cited barrier to treatment was lack of public funding. Overall, government funding for antiviral therapies for both hepatitis B and hepatitis C has improved considerably over the past decade in all four jurisdictions (see **Case study 5**). However, out-of-pocket costs are often still high for many patients, be it for diagnosis, monitoring tests [21, 34], or antiviral therapies. Funding of antiviral therapies in some countries is often limited to a given number of years, which may impact on compliance with long-term treatment regimens.

It is also important to recognise that lack of funding may sometimes be used as an excuse for not offering available treatments to patients. In truth, physicians are often

unaware of existing treatment options, or they remain unconvinced of their benefit despite their inclusion in clinical guidelines and thus adopt a 'watch and wait' approach to treatment.

ACCEPTED MANUSCRIPT

Case study 5: The importance of secure government funding for the treatment of viral hepatitis in Hong Kong

The Hong Kong government has funded antiviral therapy for hepatitis B and C since 2009 supported by annually renewable funding of approximately HKD100 million. In 2010, an additional annually renewable HKD 76 million fund was set up for hepatitis B, with an estimated 3,000 to 4,000 extra patients receiving treatment. Funding for treatment is provided to hospitals as a prospective sum. Most of the funding has gone towards hepatitis B as the number of patients with hepatitis B infection is overwhelmingly greater than those with hepatitis C infection.

This secured funding has meant that patients with hepatitis B infection are offered guaranteed funding for their treatment without any limit as to its duration, which in Hong Kong practice, means nucleos(t)ide analogue treatment for life. Physicians claim this funding has transformed their relationship with their patients. Previously, patients would resist the prescription of long-term therapy for hepatitis B due to the financial burden it posed on them. Compliance was a significant problem. Since the changes in funding, the willingness to embark on life-long treatment has increased and compliance rates have improved significantly in patients with chronic hepatitis B infection in Hong Kong.

Experts believe that it was the demonstration of the cost-effectiveness of existing treatments that helped secure the funding, as well as the existence of two regular forums on hepatitis, the Scientific Working Group on Viral Hepatitis Prevention, and the Center for Health Protection, which offer an opportunity for governments to

consult with leading liver specialists and for experts to present data to policy makers to help guide policy decisions.

4. Discussion

Medical science and public policy have reached a critical, and exciting, juncture for viral hepatitis: 179 countries worldwide have implemented vaccination programmes against hepatitis B. Up to 95% of cases of hepatitis B infection are now treatable and up to 60% of those of hepatitis C infection are curable.[27, 35, 36] Cirrhosis can be reversed [37] and treatment of liver cancer, once thought to be impossible, is now possible. Yet three-quarters of those infected with hepatitis B virus and 65% of those infected with hepatitis C virus do not know they are infected.[3] Screening uptake is low, as is uptake and adherence to treatment, with the result that outcomes for individuals infected with viral hepatitis remain suboptimal.

The CEVHAP North Asia Workshop on Viral Hepatitis highlighted the key challenges facing Hong Kong, Japan, Korea and Taiwan in their fight against viral hepatitis. These challenges are similar to those in other regions.[2, 3] The WHO Framework provides a blueprint for action, but the onus is on governments to reduce the burden posed by hepatitis locally, within the constraints and possibilities of their local epidemiology, resources, health care infrastructure and advocacy base.

The research community has an important role to play in guiding policy development on viral hepatitis. Liver specialists, in partnership with voluntary sector organisations, may help ensure that key facts about viral hepatitis – for example, that hepatitis B is treatable and hepatitis C is curable – are communicated to the media, the public and

policymakers in a way that is accessible and compelling. Social research and observational studies may help create a better understanding of the health seeking behaviours of people at risk of viral hepatitis and identify existing barriers to screening, diagnosis and proper treatment.

The WHO Framework provides a unique opportunity to countries around the world to take stock of how they have addressed the challenges posed by viral hepatitis in the past and create comprehensive, cohesive policies that may have a lasting impact. This will require a collaborative effort from primary care physicians, specialists, governments, individuals at risk and people living with viral hepatitis. Working in partnership with other more high-profile disease areas, for example non-communicable diseases, may present opportunities to raise the profile of viral hepatitis. Indeed, lessons may be learned from other disease areas – such as breast cancer, cardiovascular disease and HIV/AIDS – which have raised awareness, secured funding and developed comprehensive policies that have changed the lives of people living with the condition. The WHO Framework provides the steer to do the same for the millions of people worldwide infected with viral hepatitis.

Acknowledgements:

This paper draws from discussions held at the CEVHAP North Asia Forum, held in Taipei, Taiwan, in October 2012. The workshop was made possible through unrestricted grants and core funding from Bristol-Myers Squibb, Merck, Gilead and Janssen. This publication was funded by CEVHAP as part of this workshop.

ACCEPTED MANUSCRIPT

Reference List

- [1] World Health Organisation. Prevention and control of viral hepatitis infection: a framework for global action. Geneva: World Health Organisation; 2012.
- [2] Hatzakis A, Wait S, Bruix J, Dusheiko G, Esmat G, Esteban R, et al. The state of hepatitis B and C in Europe: report from the hepatitis B and C summit conference. *Journal of Viral Hepatitis* 2011;18(Suppl 1):1-16.
- [3] Institute of Medicine. Hepatitis and liver cancer: a national strategy for prevention and control of hepatitis B and C. Washington D.C.: The National Academies Press; 2010.
- [4] World Health Organization. Hepatitis B Fact sheet N°204. 2012.
- [5] Sievert W, Altraif I, Razavi HA, et al. A systematic review of hepatitis C virus epidemiology in Asia, Australia and Egypt. *Liver International* 2011;31 Suppl 2:61-80.
- [6] Wang W-L, Want C-J, Tseng H-F. Comparing knowledge, health beliefs and self-efficacy towards hepatitis B prevention among university students with different hepatitis B virus infection statuses. *J Nursing Research* 2009;17:10-19.
- [7] IMS Health Taiwan. Taiwan hepatitis B disease awareness and attitude in general population. 2005.
- [8] de Martel C, Ferlay J, Franceschi S, Vignat J, Bray F, Forman D, et al. Global burden of cancers attributable to infections in 2008: a review and synthetic analysis. *Lancet Oncology*, Published online May 9, 2012, DOI:10.1016/S1470-2045(12)70137-7
- [9] Centers for Disease Control. Know More Hepatitis. 2013.
- [10] Ward J, Lok A, Thomas DI, El-Serag HB, Kim WR. Report on a single-topic conference on "Chronic viral hepatitis-strategies to improve effectiveness of screening and treatment.". *Hepatology* 2012;55:307-315.
- [11] Ly KN, Xing J, Klevens RM, Jiles RB, Ward JW, Holmberg SD. The Increasing Burden of Mortality From Viral Hepatitis in the United States Between 1999 and 2007. *Annals of Internal Medicine* 2012;156:271-278.
- [12] Tanaka J, Koyama T, Mizui M, Uchida S, Katayama K, Matsuo J, et al. Total Numbers of Undiagnosed Carriers of Hepatitis C and B Viruses in Japan Estimated by Age- and Area-Specific Prevalence on the National Scale. *Intervirology* 2011;54:185-195.
- [13] Butler J, Korda RJ, Watson K, Watson D. The impact of hepatitis B in Australia: Projecting mortality, morbidity and economic impact. Canberra, Australia: Australian Centre for Economic Research on Health; 2009.
- [14] Japan Hepatitis Council survey 2012. 2013.
- [15] Report of the epidemiological research group on viral hepatitis, supported by the Ministry of Health and Welfare in Japan. 2011.
- [16] Katamaya K, et al. Report of questionnaire survey about the rate of having hepatitis screening and the prevalence of hepatitis virus infection among the general population and the working population. *Kanzo* 2012;53:707-720.
- [17] Nelson PK, Mathers BM, et al. Global epidemiology of hepatitis B and hepatitis C in people who inject drugs: results of systematic reviews. *Lancet* 2011;378:571-583. Epub 2011 Jul 27.
- [18] Amin J, Law MG, Bartlett M, Klador JM, Dore GJ. Cause of death after diagnosis of hepatitis B or hepatitis C infection: a large community-based linkage study. *Lancet* 2006;368:938-945.
- [19] Kourtis AP, Bulterys M, Hu DJ, Jamieson DJ. HIV-HBV Coinfection - a global challenge. *New England Journal of Medicine* 2012;366:1749-1752.
- [20] Ishikawa T, et al. Outbreak of hepatitis C virus infection in an outpatient clinic. *J Gastroenterol Hepatol* 2005;7:1087-1093.

- [21] Farrell GC. New hepatitis C guidelines for the Asia-Pacific region. APASL consensus statements on the diagnosis, management and treatment of hepatitis C virus infection. *J Gastroenterol Hepatol* 2007;23:607-610.
- [22] McCaughan GW, Omata M, Amarapurkar X., et al. Asian Pacific Association for the Study of the Liver consensus statements on the diagnosis, management and treatment of hepatitis C virus infection. *J Gastroenterol Hepatol* 2007;22:615-633.
- [23] Kumagai J, Komiya K, et al. Hepatitis C virus infection in 2,744 hemodialysis patients followed regularly at nine centers in Hiroshima during November 1999 through February 2003. *J Med Virol* 2005;76:498-506.
- [24] Chen DS, Hus N-H, Sung J-L, et al. A mass vaccination program in Taiwan against hepatitis B virus infection in infants of hepatitis B carrier-mothers. *JAMA* 1987; 257[19]: 2597-603. *JAMA* 1987;257[19]:2597-2603.
- [25] Wait S, Chen DS. Towards the eradication of hepatitis B in Taiwan. *Kaohsiung J Med Sci* 2012;28:1-9.
- [26] Chien Y-C, Jan C-F, Kuo H-S, Chen CJ. Nationwide Hepatitis B vaccination program in Taiwan: Effectiveness in the 20 years after it was launched. *Epidemiol Rev* 2006;28:126-135.
- [27] Chang MH, You S-L, Chen CJ, Liu C-J, Lee C-M, Lin S-M, et al. Decreased Incidence of Hepatocellular Carcinoma in Hepatitis B Vaccinees: A 20-Year Follow-up Study. *J of the National Cancer Institute* 2009;101:1348-1355.
- [28] Chen DS. Hepatitis B vaccination: the key towards elimination and eradication of hepatitis B. *J Hepatol* 2009;50:805-816.
- [29] Chen DS. Hepatocellular carcinoma in Taiwan. *Hepatol Res* 2007;37:S101-S105.
- [30] Lu SN, Chen CH, Chen TM, Lee PL, Wanga J-H, Tunga H-D, et al. Hepatitis B virus infection in adolescents in a rural township—15 years subsequent to mass hepatitis B vaccination in Taiwan. *Vaccine* 2006;6:759-765.
- [31] Chang MH, Chen TH, Hsu HM, Wu TC, Kong MS, Liang DC, et al. Prevention of hepatocellular carcinoma by universal vaccination against hepatitis B virus: the effect and problems. *Clin Cancer Res* 2005;11:7953-7957.
- [32] Lee L-T, Huang H-Y, Huang K-C, Chen C-Y, Lee W-C. Age-period cohort analysis of hepatocellular carcinoma mortality in Taiwan 1976-2005. *Ann Epidemiol* 2009;19:323-328.
- [33] Knott A, Dieperink E, Willenbring ML, et al. Integrated psychiatric/medical care in a chronic hepatitis C clinic: effect on antiviral treatment evaluation and outcomes. *Am J Gastroenterol* 2006;101:2254-2262.
- [34] Liaw YF, et al. Asian-Pacific consensus statement on the management of chronic hepatitis B: a 2008 update. *Hepatol Int* 2008;2:263-283 Epub 2008 May.
- [35] Janssen H, van Zonneveld M, Senturk H, et al. Pegylated interferon alfa-2b alone or in combination with lamivudine for HB3Ag-positive chronic hepatitis B: a randomised trial. *Lancet* 2005;365:123-129.
- [36] Veldt BJ, Heathcote EJ, Wedemeyer H, et al. Sustained virologic response and clinical outcomes in patients with chronic hepatitis C and advanced fibrosis. *Ann Intern Med* 2007;147:677-684.
- [37] Mallet V, Gigenkrantz H, Serpaggi J, et al. Brief communication: the relationship of regression of cirrhosis to outcome in chronic hepatitis C. *Ann Intern Med* 2008;149:399-403.
- [38] Fung J, Yuen M-F. This is hepatitis -- it is closer than you think. *Indian J Med Res* 2012 ;136:3-6.

Table 1 Epidemiology of hepatitis B and hepatitis C in Hong Kong, Japan, Korea and Taiwan

Country	Hepatitis B			Hepatitis C			Hepatocellular carcinoma (HCC)			
	Prevalence of chronic hepatitis B infection, general population (%)	Estimated number of carriers (millions)	Age group with highest number of carriers	Prevalence in general population (%)	Dominant genotype	Time trends	Incidence in men; women (rate per 100,000 persons)	% due to hepatitis B infection*	% due to hepatitis C*	Median age of onset
Hong Kong [41]	8.8	0.7	>20 years (prevalence increases with age)	0.30%	1b, 6a	Very low prevalence, most common in IDUs.	29.9; 8.3	75-80	3-6 ⁴⁴	63 for men, 71 for women
Japan [12;20;42]	0.71	0.9	50-64 years	0.63%	70% 1b, 20% 2a, 10% 2b	Risk factors changing over time and by region.	2.42; 1	15%	67.70%	66.4 for men, 69.9 for women
Korea [43]	2.8	2.25-2.27	30-50 years	1.29 (in >40 population)	1b, 2a	Mostly >40 age group people. Lack of data on youth, little data on role of injecting drug use.	45; 33.6	20	72	Incidence increases after age 40, peak at 55
Taiwan [30;44]	10-12%	2.5-3	35 (or 40)-55 (or 60) years	4.4% (>20 y.o)**	1b, 2a	Most disease in older groups. Significant geographic variations (from 0-90% depending on village)(45)	53; 21	53(30)	28 (8% due to B+C)(30)	58 average, mean age 10 years lower for HBV vs. HCV-caused HCC.***

HCC: hepatocellular carcinoma. IDU: injecting drug users

* The remainder of cases of HCC is caused by alcohol and other factors such as aflatoxin.

** This data is from populations participating in screening programmes only.

*** One would expect the relative proportion of HCV-related HCC and the age of onset of HCC to increase in future

ACCEPTED MANUSCRIPT

Table 2: Priorities for action in Hong Kong, Japan, Korea, and Taiwan according to the four strategic axes of the WHO Global Framework

Priorities for action
1. Raising awareness, promoting partnerships and mobilizing resources
Greater public awareness
Greater awareness of primary care physicians
Building patient advocacy
Strengthening hospital-primary care networks
2. Evidence-based policy and data for action
Economic data on the burden of viral hepatitis
Better data on barriers to screening and treatment
Centralised surveillance
Accurate estimates of the number of chronic hepatitis cases
3. Prevention of transmission
Better monitoring of vaccine effectiveness
Universal vaccination of children and improved access to vaccination by people at greater risk
Targeted harm reduction strategies
Better data on vaccine failure
4. Screening, care and treatment
Improved availability and funding of screening [public funds and/or employer-based]
Linking screening to effective monitoring and treatment
Funding screening for hepatocellular carcinoma
Improved access to treatment of chronic hepatitis and hepatocellular carcinoma

Table 3: Barriers to screening linked to individuals, providers and the healthcare system

Source of barrier	Barriers
Individuals	Unaware that one is at risk of viral hepatitis Unaware that the disease can have serious long-term effects Unaware that effective treatments exist Cultural beliefs Stigma associated with viral hepatitis Costs associated with testing [lack of funding]
Health care providers	Social stigma Poor understanding of the availability and effectiveness of treatment Lack of disease management approach – ‘wait and see’ attitude to viral hepatitis Cost barriers to access treatment Lack of awareness about the need for monitoring [hepatitis B]
Healthcare system	Lack of continuity / no linkage from screening to care Cost of therapy / lack of government reimbursement

Adapted from: [38]

Fig. 1. The four strategic axes for policy development recommended in the WHO Prevention & Control of Viral Hepatitis Infection: Framework for Global Action

Fig. 2. Example of a diorama on viral hepatitis at a US airport

Fig. 3. Incidence of HCC by age in cohorts born before and after infant vaccination programme against hepatitis B virus in Taiwan (started in 1984) [27]





ACCEPTED MANUSCRIPT

