

Regional strategy  
for the prevention  
and control of **viral hepatitis**



**World Health  
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Regional Office for South-East Asia



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# Regional strategy for the prevention and control of viral hepatitis

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# Abbreviations

AASLD	American Association for Study of Liver Diseases
ALT	alanine aminotransferase
APASL	Asia Pacific Association for the Study of the Liver
ART	antiretroviral therapy
DAA	direct-acting antiviral agent
DTP	diphtheria, tetanus, pertussis
EASL	European Association for the Study of Liver
EIA	enzyme immunoassay
EPI	Expanded Programme on Immunization
FHF	fulminant hepatic failure
HAV	hepatitis A virus
HBcAg	hepatitis B core antigen
HBsAg	extracellular hepatitis B antigen
HBsAg	hepatitis B surface antigen
HBV	hepatitis B virus
HCC	hepatocellular carcinoma
HCV	hepatitis C virus
HDV	hepatitis delta virus
HepB	hepatitis B (vaccine)
HEV	hepatitis E virus
Hib	Haemophilus influenzae type b
IgM	immunoglobulin M

JIF	joint reporting form
NGO	nongovernmental organization
NIP	national immunization programme
PATH	Programme of Advancement Through Health and Education
PEP	post-exposure prophylaxis
RC-VHLD	referral centre for viral hepatitis laboratory diagnosis
RC-VHSPC	referral centre for viral hepatitis surveillance, prevention and control
RT-PCR	reverse transcriptase polymerase chain reaction
SGP	Small Grants Programme
STI	sexually transmitted infection
SVR	sustained virological response
TB	tuberculosis
UNICEF	United Nations Children's Fund
USA	United States of America
WHO	World Health Organization

# Executive summary

Viral hepatitis, caused by infection with one of the hepatitis viruses, is a major public health problem worldwide. In May 2010, the World Health Assembly adopted a resolution (WHA63.18) that called for comprehensive prevention and control strategies for viral hepatitis (1). In particular, the Assembly requested the World Health Organization (WHO) to develop, in collaboration with Member States, necessary measures, guidelines, strategies, time-bound goals and tools for the surveillance, prevention and control of viral hepatitis. In view of this, the WHO Regional Office for South-East Asia organized two informal consultations (in June 2010 and April 2012) on viral hepatitis to: (i) review the current status of disease burden, and prevention and control activities; (ii) identify priorities for research, policy and action; and (iii) develop a strategy for improved prevention and control of viral hepatitis, in the South-East Asia Region (2, 3).

A review of available data reveals that infection with various hepatitis viruses, A–E, is common in the South-East Asia Region. Among enterically transmitted viruses, seroprevalence rates for hepatitis A virus are high in most countries in the Region, but with a recent decline. The consequent increase in average age at first exposure has led to an increase in the number of clinical cases of hepatitis A, including severe forms of disease. A vaccine against hepatitis A is available but it is not yet being used as a public health measure in the Region. Infection with hepatitis E virus is highly endemic in several countries and causes frequent waterborne outbreaks and nearly half of all cases of acute viral hepatitis in many countries. Rapid urbanization, with limited access to safe drinking water and food and proper sanitation, adds to the risk of these infections.

Among bloodborne hepatitis viruses, infection rates for hepatitis B virus vary between low, intermediate and high among various countries in the Region. Infection rates for hepatitis C virus in the Region vary from 1% to 3%. Infection with either of these viruses can be persistent. Persistent infection with these viruses, though often asymptomatic, can lead to development of cirrhosis and liver cancer, which account for

a large number of deaths in the Region. These infections are more common in some specific population groups, e.g. injecting drug users, recipients of blood transfusions and immunosuppressed persons (including those with HIV infection). It is estimated that the Region has nearly 100 million and 30 million people with chronic hepatitis B and hepatitis C virus infection, respectively. Universal immunization of all neonates for hepatitis B, including a 'birth dose', has been introduced in all countries; however, the coverage rates remain low in some areas. Also, screening of blood and blood products for agents that cause viral hepatitis is lacking in some areas.

Thus, infection with hepatitis viruses causes a significant disease burden in the South-East Asia Region, in the form of both acute and chronic hepatitis, with approximately 500 000 deaths annually in the Region. However, the available data from the Region on rates of infection with hepatitis viruses, rates of clinical disease caused by these viruses, and the associated morbidity and mortality, are limited and fragmentary and may not provide a complete picture. Further, there are no data on the societal and economic impact (in terms of years of life lost, disability, loss of productivity, expenditure on medical care, etc.) of these infections in the Region (4).

The problems associated with viral hepatitis in the Region include:

- low levels of awareness among health administrators and policy-makers, medical professionals and the general population about hepatitis viruses, including their routes of transmission, risk factors and impact on human health;
- inadequate disease surveillance systems, with a high likelihood of underreporting of both acute and chronic infections, leading to insufficient understanding of the magnitude and seriousness of the public health problems associated with viral hepatitis;
- limited knowledge, availability of, access to and use of preventive services for viral hepatitis, including screening of transfused blood and blood products;
- rapid urbanization, overpopulated cities and lack of access to clean water and sanitation;
- limited testing facilities for detection of chronic hepatitis B or C infection, leading to a large proportion of persons with chronic infection remaining undiagnosed;

- the high cost of and inadequate access to treatment for viral hepatitis and for its long-term complications (cirrhosis and liver cancer) and liver transplantation in patients with end-stage disease;
- inadequate financial and manpower resource allocation and public spending on programmes for surveillance, prevention and control of viral hepatitis, leading to insufficient understanding of the extent and seriousness of this public health problem;
- low rates of infant hepatitis B vaccine coverage, particularly for the dose at birth, in some parts of the Region.

To reduce the incidence of infections with hepatitis viruses, and to reduce morbidity and mortality due to viral hepatitis and its complications, it is essential to develop a strategy to comprehensively address these issues.

To formulate the *Regional strategy for the prevention and control of viral hepatitis*, six pillars have been identified:

- (1) strategic framework for policy, planning, advocacy and resource mobilization;
- (2) strategic framework for surveillance;
- (3) strategic framework for research;
- (4) strategic framework for prevention and control;
- (5) strategic framework for education;
- (6) strategic framework for medical care and treatment.

These regional frameworks are aligned with the four strategic axes of WHO's global comprehensive approach in the prevention and control of viral hepatitis (5), as shown in Table 1.

Viral hepatitis requires high-level consideration in terms of governments' awareness and commitment, and adequate allocation of resources from governments for prevention and control.

The WHO Regional Office for South-East Asia will pursue the goals and strategies of the regional viral hepatitis prevention and control strategy by supporting programme and policy development. The success of the plan requires a coordinated, collaborative and sustained approach for viral hepatitis prevention, education, surveillance, medical

Table 1: Comparison of WHO’s strategic axis and the South-East Asia Region Strategic Frameworks

WHO’s strategic axis (5)	Regional strategic framework
1. Partnership, mobilization and communication	1. Policy, planning, advocacy and resource mobilization (building the infrastructure for sound policy and programme development)
2. Data for policy and action	2. Surveillance 3. Research for improvement of the viral hepatitis prevention and control programmes
3. Prevention of transmission	4. Prevention (promoting risk reduction, safe health care, screening blood and blood products, safe medical manipulations/injections and hepatitis B virus vaccination) 5. Education (improved knowledge and awareness)
4. Screening, care and treatment	6. Medical care and treatment (assuring timely access to care, treatment and other related services for patients with acute and chronic viral hepatitis)

care and treatment, research, policy, planning and resource mobilization. The WHO Regional Office for South-East Asia will engage and facilitate the involvement of Member States, ministries of health and governmental and nongovernmental organizations and institutions in carrying out the necessary activities to achieve the goals and strategies of the regional strategy. By aligning activities with the regional strategy, the countries of the Region will maximally utilize opportunities to prevent new hepatitis A, B, C and E infections and improve the quality of life of individuals living with chronic hepatitis B and C.

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# 1. Introduction

Hepatitis means “inflammation of the liver”. Five types of viruses can cause viral hepatitis. Of these, the most common cause of infection is one of four viruses: hepatitis A, B, C or E. Hepatitis D, also referred to as hepatitis D virus, or hepatitis delta virus (HDV) is considered to be a subviral satellite because it can propagate only in the presence of the hepatitis B virus (HBV). All or any of these viruses can cause an acute disease, with symptoms lasting several weeks, including yellowing of the skin and eyes (jaundice), dark urine, extreme fatigue, nausea, vomiting and abdominal pain. It can take several months to a year to feel fit again. Easily contracted in many ways, from drinking water to casual contact or sexual intercourse, this debilitating disease poses a risk to everyone. A summary of viral hepatitis transmission, risk activities, prevention and treatment is presented in *Annex 1*.

## **2. Viral hepatitis in the countries of the World Health Organization South-East Asia Region**

### **2.1 Hepatitis A**

In the World Health Organization (WHO) South-East Asia Region, the annual number of acute cases of hepatitis A is estimated to be 400 000, with 800 deaths. In the 1980s, the presence of the anti-hepatitis A virus antibody (anti-HAV) was detected in more than 90% of children aged 15 years, and almost everyone above 25 years of age in the WHO South-East Asia Region, indicating that they had been infected with hepatitis A virus (1). However, in the past 5 years, it has been observed that with the improvement of sanitary conditions in some countries, many children have not become infected with HAV in early childhood. Sero-epidemiological studies conducted in Bangladesh, India, Sri Lanka and Thailand have indicated a decline in anti-HAV prevalence among school children, which increases the possibility of an outbreak of HAV infection among urban school children (2–6). The shifting of an epidemiological pattern from high to intermediate endemicity paradoxically leads to higher disease incidence of hepatitis A, as infections occur in the older age groups, and reported rates of clinically evident hepatitis A are higher. In recent years, a tendency of increase of severe manifestation of hepatitis A with failure of liver function among children, and more cases in adults, has been observed in the countries in the Region (4, 7, 8).

### **2.2 Hepatitis B**

There are approximately 100 million hepatitis B carriers in the South-East Asia Region, and they account for more than 5.6% of the global population. More than 300 000 people are estimated to die each year in the Region as a result of the chronic

consequences of hepatitis B, particularly cirrhosis and liver cancer. Table 2 summarizes findings on the prevalence of hepatitis B. This reflects a low prevalence of less than 1% in two countries – Nepal (10–11) and Sri Lanka (9); intermediate prevalence (2–6%) in seven countries – Bangladesh (13–16), Bhutan (17, 18), Democratic People's Republic of Korea (1, 17), India (19–26), Maldives (27), Thailand (28–33) and Timor-Leste (17; and high prevalence (more than 10%) in two countries – Indonesia (34–38) and Myanmar (39–42).

Table 2:

Country	Prevalence of hepatitis B surface antigen (HBsAg) (%)	
	Source: publications, presentations and documents, 1980–1999	Source: publications, presentations and documents, 2000–2010
Bangladesh	12 (13,14)	5–6.9 (15, 16)
Bhutan	6.1 (18)	4.7 (17)
Democratic people's Republic of Korea	10 (1)	4.7 (17)
India	5–7 (21)	3–4.2 (19, 26)
Indonesia	9–10.5 (34, 35)	11–15.5 (36–38)
Maldives	6.5 (27)	
Myanmar	10–13 (39, 40)	12 (42)
Nepal	1 (9)	0.8–1.5 (10, 11)
Sri Lanka	1 (1)	0.46 (17)
Thailand	8–9 (28, 30)	2.8–4.5 (33)
Timor-Leste		6.9 (17)

There are 10 known HBV genotypes, classified from A to J (43). Type A is prevalent in Europe, Africa and South-East Asia. Types B and C are predominant in Asia. Type D is common in the Mediterranean area, the Middle East and India. Type E is localized in sub-Saharan Africa. Type F (or H) is restricted to Central and South America. Type G has been found in France and Germany. Genotypes A, D and F are predominant in Brazil, and all genotypes occur in the United States of America, with frequencies dependent on ethnicity. The E and F strains appear to have originated in aboriginal populations of Africa and the New World, respectively. Within genotypes, 24 subtypes have been described, which differ by 4–8 % of the genome (44).

The majority of studies showing association of genotypes in disease progression are from South-East Asia, where HBV infection itself is hyperendemic and there is a preponderance of genotypes B and C, except in India, where the most common genotype is D, followed by A and C. HBV genotypes B and C are predominant in Thailand. Infection with genotype C is more common than with genotype B. Patients with genotype C infection had a higher positive rate of the extracellular antigen (HBeAg) and exhibited earlier progression of cirrhosis and hepatocellular carcinoma (HCC) than those with genotype B infection. However, there were no differences between patients with these genotypes in the risk of developing HCC and its prognosis (45).

Studies conducted in South-East Asia suggest important pathogenic differences between HBV genotypes, which may contribute to more severe liver disease, including cirrhosis and HCC, and genotype C and D HBV infections. In addition, patients with genotype A or B infection respond better to interferon-based therapy than those with genotype C or D infection. Therefore, the genotype and chronic HBV infection can help physicians to identify those at risk of disease progression and determine the optimal antiviral therapy (46–49).

It is important to mention hepatitis D or delta hepatitis, which is caused by the hepatitis delta virus (HDV), a defective RNA virus. HDV requires the help of HBV to replicate (50). HDV is transmitted in the same way as HBV. Blood is potentially infectious during all phases of active hepatitis D infection. Peak infectivity probably occurs just before the onset of acute disease. Chronic HBV carriers are at risk for infection with HDV.

Individuals who are not infected with HBV, and have not been immunized against HBV, are at risk of infection with HBV with simultaneous or subsequent infection with HDV. The hepatitis delta virus is present worldwide and in all age groups. Its distribution parallels that of HBV infection, although with different prevalence rates (highest in parts of Romania, the Russian Federation, Southern Italy and the Mediterranean countries, Africa and South America). In countries with high HBV prevalence, such as China, HDV infection is disproportionately low. In the WHO South-East Asia Region, Bangladesh, India and Thailand have reported relatively moderate HBV coinfection with HDV (51–54), particularly among injecting drug users (55). HDV infection of chronically infected HBV carriers may lead to fulminant acute hepatitis or severe chronic active hepatitis, often progressing to cirrhosis. Chronic hepatitis D may also lead to the development of HCC. Since HDV is dependent on HBV for replication, control of HDV infection is achieved by targeting HBV infections.

Despite the large number of publications on the prevalence of hepatitis B in the countries of the South-East Asia Region, there is a lack of accurate prevalence data for viral hepatitis. This links directly to limited access to testing – more than half the population in the Region lives in countries with no provision for free testing.

Since 1976, Member States of the WHO South-East Asia Region have identified liver diseases as one of the leading regional health priorities and have requested WHO to provide technical support in conducting epidemiological studies on viral hepatitis, developing diagnostic reagents and tests, and developing and producing the hepatitis B vaccine (1).

A hepatitis B control programme is multifaceted and may involve immunization, blood screening, injection safety, public health awareness and education, sexual health programmes, surveillance, drug and alcohol services, and access to blood testing and treatment. Strategic planning and coordination are therefore essential.

All South-East Asia Region countries consider hepatitis B as an urgent public health issue and have a policy and plan, but in most Member States implementation is not adequate, and sometimes follows a series of uncoordinated programmes rather than a cohesive strategic approach.

Some countries have not been able to implement the mandatory HBsAg screening of blood and blood products, and blood transfusion without screening is still practised. Currently no governmental funding exists for treatment of patients with chronic hepatitis B. In addition to access to testing, improving diagnosis requires awareness of the risks and routes of transmission among those who may have been exposed to HBV. This is also crucial for prevention. However, government-funded public awareness work is not regular and more effort and resources are required.

In addition to the governments' efforts, in certain countries civil society and nongovernmental organizations (NGOs) are involved in promotion of HBV vaccination. Their participation could be effectively used for the prevention and control of hepatitis B infection. Clearly, in settings where they are active, a better coordination with the national health authorities is crucial.

## **Hepatitis B immunization**

In all countries in the South-East Asia Region, much progress has been made in protecting the next generation from hepatitis B, and to date more than 130 million infants have received three doses of the HBV vaccine. The limited availability of the hepatitis B

vaccine for national immunization programmes, largely due to cost, has been an obstacle that has recently been overcome by all countries in the South-East Asia Region, some with financial assistance from the GAVI Alliance in the first 5 years of use.

Indonesia and Thailand introduced the hepatitis B (HepB) vaccine before the 1992 World Health Assembly resolution recommending hepatitis B vaccination worldwide (33, 56). Introduction of the HepB vaccine in Indonesia was based on the accumulated evidence presented earlier. The introduction was phased, beginning with the island of Lombok in 1987, with collaboration between the ministry of health, the Programme of Advancement Through Health and Education (PATH) and the International Task Force on Hepatitis B Immunization. After 4 years of implementation, a decrease in the prevalence of HBsAg among children below 4 years of age was observed – from 6.2% to 1.4% (57). This evidence was used to expand the programme nationally with strong government support and funding. The trial was started using monovalent HBV vaccine in multidose vials. This was replaced with Uniject monovalent vaccine for all three doses, which was later replaced with Uniject for the dose at birth, followed by combination diphtheria, tetanus, pertussis (DTP)–HepB for three additional doses. Use of the pentavalent vaccine with a combination of DTP–HepB–Hib (*Haemophilus influenzae* type b) has been planned in Indonesia.

Thailand initiated hepatitis B vaccination in a pilot phase in two provinces in 1989, which was then scaled up to include 12 more provinces, and by 1992 HepB vaccine was integrated into its Expanded Programme on Immunization (EPI) nationwide. The impact of vaccination has been reviewed at regular intervals and excellent data exist to show the dramatic impact of the vaccination on the prevalence of HBsAg in Thailand. In the initial pilot in Chonburi and Chiang Mai, within 4 years of the introduction of the HepB vaccination, the prevalence of HBsAg dropped from 5.4% in 1988 to 0.8% in 1993, representing an 85% reduction in the prevalence of HBsAg. A 12-year review conducted in 2006 showed that the prevalence of HBsAg in children below the age of 18 years declined from 4.3% to 0.7% and the prevalence of anti-HBC dropped from 15.8% to 2.9% (58). The impact of universal HepB vaccination, namely drastic reduction of HBV carrier status among vaccinated children in Thailand, has become one of the motivating factors for all South-East Asia Region Member States to intensify and expand HepB vaccination.

In high- and intermediate-prevalence countries, most infections occur by mother-to-child transmission at birth, from chronically infected mothers, when the risk of chronic infection is the highest (approximately 90%), or from person to person in early childhood. Therefore, whenever possible, vaccination starting at birth is the most

important prevention strategy. However, for programmatic reasons, HepB vaccination is easily administered as a combination vaccine together with the DTP vaccination, starting at 6 weeks of age. Giving a dose at birth requires purchase and storage of two different types of vaccines (monovalent and combined) but it is being practised effectively at least in four Member States in the Region.

Following the launch of the GAVI Alliance, countries in this Region have taken advantage of the support provided by GAVI to introduce the hepatitis B vaccine into their routine national immunization programmes (NIPs). Currently, all SEAR Member States have the hepatitis B vaccine in their routine NIPs, with six of them including a dose at birth.

- Bangladesh introduced the HepB vaccine in a phased manner, starting in 2002 and reaching nationwide coverage by 2004. It now uses the pentavalent vaccine at 6, 10 and 14 weeks, since 2009 (no dose at birth).
- Bhutan introduced a plasma-derived hepatitis B vaccine in 1997, but in 2002, with GAVI support, it switched first to DNA recombinant vaccine, and in 2004 switched again to the DTP–HepB (tetraivalent) formulation and to pentavalent vaccine in 2009. The schedule is also 6, 10 and 14 weeks with limited coverage of a dose at birth.
- The Democratic People’s Republic of Korea also introduced HepB vaccine from 2002, with support from the GAVI Alliance, and implementing a dose at birth.
- Maldives had introduced HepB vaccine before the formation of GAVI Alliance. Vaccination is started at birth and has reached a very high coverage.
- Myanmar introduced the HepB vaccine in a phased approach in July 2003, covering the whole country in 2005, including a dose at birth.
- Nepal also introduced HepB vaccine in 2002, first using only monovalent HepB but switching to the combination DTP–HepB formulation during 2005–2006. It now uses the pentavalent vaccine, without a dose at birth.
- Sri Lanka, also using GAVI support, introduced HepB vaccine from 2003, with a phased approach. It now uses the pentavalent vaccine, without a dose at birth.
- Timor-Leste introduced HepB in 2006. It is now using DTP–HepB and will soon switch to pentavalent vaccine.

- India, with the largest birth cohort in the world, introduced HepB vaccine coverage to all parts of the country in 2011. The pilot-based introduction of HepB started in India in 2002–2003 in 33 districts and 15 municipalities.

In all countries where HepB has been introduced in the EPI routine immunization programme for infants, it has been accepted well by both the community and health-care workers, and coverage is 71.5% (see Table 3 and Figures 1 and 2). The situation regarding vaccination of high-risk groups (injecting drug users, health-care workers, dialysis patients) is not coordinated and monitored systematically.

## 2.3 Hepatitis C

The WHO South-East Asia Region has about 30 million hepatitis C carriers, which is more than 1.6% of the total population. Over 120 000 infected individuals in the Region are estimated to die each year, as a result of cirrhosis and liver cancer associated with hepatitis C (59), and this infection is considered a significant and growing public health problem. Transfusion of unsafe blood, use of non-sterile syringes and equipment, injecting drug use, and repeated haemodialysis are major known causes of transmission of HCV in the Region's countries. Although many blood banks in the Region screen blood for HIV and HBV, they often do not have the resources to screen for HCV.

Six major HCV genotypes and numerous subtypes have been identified. The major HCV genotype worldwide is genotype 1. Genotypes 2 and 3 are also found globally and account for a significant minority of infections. The other genotypes have a more specific geographic distribution. Genotype 3 is found in Australia, the Indian subcontinent and Thailand. Genotype 4 is the most prevalent genotype in Egypt and the Middle East. Genotype 5 is found in South Africa, and genotype 6 is more common in Hong Kong, Macao, and Viet Nam (60–62).

In countries of the WHO South-East Asia Region, injecting drug use is also widespread. Bangladesh, India, Indonesia, Myanmar, Nepal and Thailand also have a high prevalence of HIV and HCV infection and 50–100% of HIV-positive injecting drug users are coinfecting with HCV (63–89).

All countries in the Region share common challenges regarding hepatitis C. The most important one is a very low level of awareness about the severity of the problem among the general population, as well as public health professionals. In addition, clinical knowledge of HCV worldwide also seems inadequate (90–103).



Table 3: Number of children immunized with HepB3\* vaccine by country and year 2003–2011

Countries	2003	2004	2005	2006	2007	2008	2009	2010	2011	Total
Bangladesh	171 676	375 595	2 319 200	3 566 628	3 676 487	3 750 099	3 469 139	3 500 025	3 587 704	24 416 553
Bhutan	—	13 355	13 710	13 400	12 674	13 072	13 382	12 625	12 796	105 014
Democratic People's Republic of Korea	114 037	413 734	367 787	392 746	385 273	391 485	317 559	321 875	322 729	3 027 225
India	—	1 280 000	1 570 000	1 641 890	1 290 959	5 825 697	9 169 827	9 399 985	12 311 340	42 489 698
Indonesia	3 750 880	3 822 089	2 942 140	3 494 272	4 475 611	4 456 263	4 530 192	4 540 904	4 469 678	36 482 029
Maldives	5 921	5 051	5 105	5 701	5 702	5 909	10 346	10 542	7 071	61 348
Myanmar	108 754	535 828	863 492	868 779	1 194 772	1 255 212	1 340 888	1 357 203	581 624	8 106 552
Nepal	18 386	196 596	398 751	661 584	630 718	615 267	613 167	529 310	627 998	291 777
Sri Lanka	108 773	227 140	310 030	330 374	341 735	341 579	329 870	334 153	337 976	2 661 630
Thailand	ND	ND	ND	ND	ND	ND	ND	ND	ND	—
Timor-Leste	—	—	—	25 374	28 311	30 452	32 542	30 524	28 281	175 484
South-East Asia Region total	4 278 427	6 869 388	8 790 215	11 000 748	12 042 242	16 685 035	19 826 912	20 037 146	22 287 197	121 817 310

ND, no data.

Source: WHO/United Nations Children's Fund (UNICEF) joint reporting form (JIF).

\*HepB3 is common definition used by WHO/UNICEF which means Third dose of HepatitisB (child which had only one or two doses of vaccination is not counted)

Figure 1: Number of children immunized with HepB3 vaccine by year, South-East Asia Region, 2003–2011

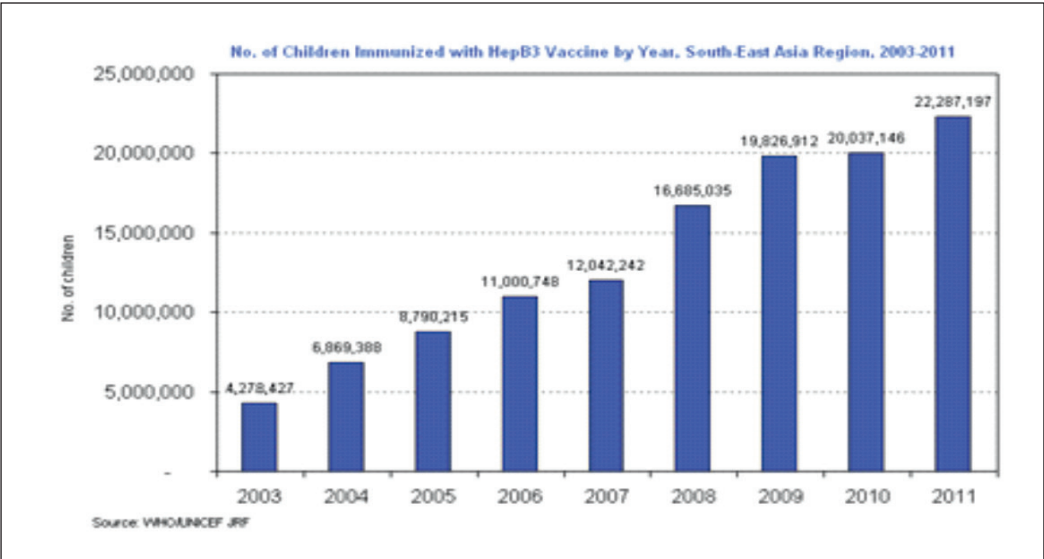
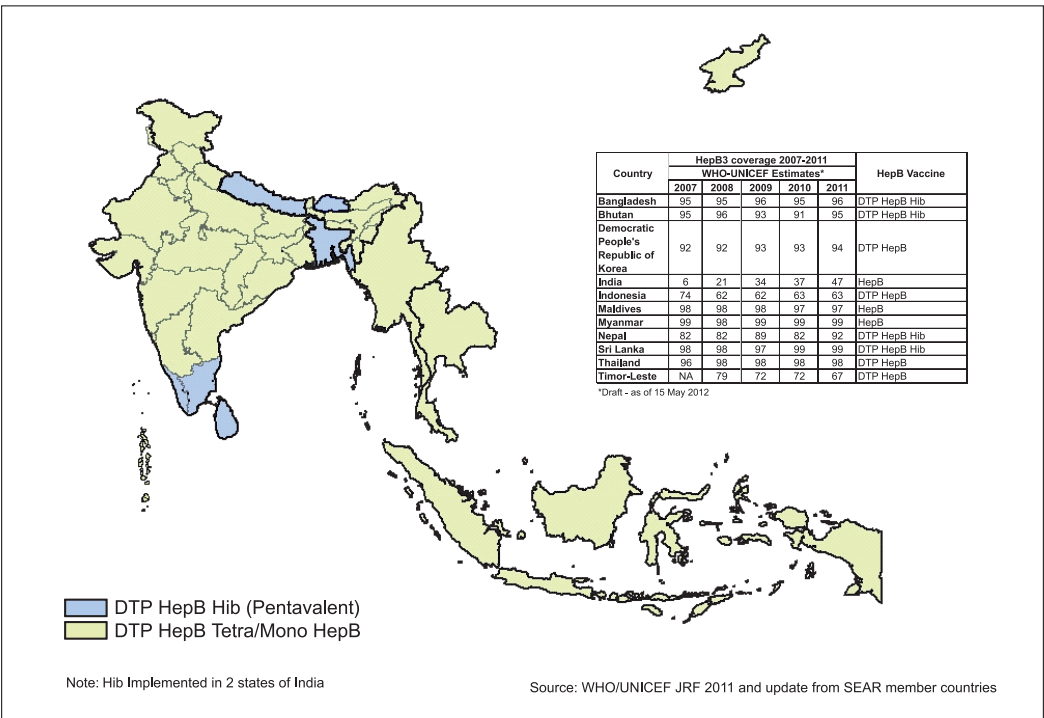


Figure 2: Implementation and coverage of HepB vaccination in the South-East Asia Region, 2007–2011



Comparisons of HCV with HIV are nearly unavoidable – both appeared on the communicable disease radar around the same time and both have similar modes of transmission. However, the HCV issue cannot be solved through the agents developed to fight HIV, given the marked differences in the biology of these viruses. Their differences are greater than their similarities. HCV has been endemic to human populations for centuries. The differences also stretch beyond biology and into public health initiatives. The discovery of HIV led to a large amount of funding for antiviral research and development around the world. With hepatitis C, screening blood and blood products, as well as clinical diagnosis of this infection have lagged far behind the processes for HIV (104).

### Coinfections with HIV and hepatitis viruses

The prevalence of HBV and HCV coinfection is up to 60% among persons living with HIV infection. All these infections have a similar route of transmission and are more prevalent in the South-East Asia Region, and hence require special attention (105–108). Coinfected individuals have more rapid progression of liver disease and a greater probability of developing cirrhosis and liver cancer (109, 110). Furthermore, treatment of HCV infection is often recommended before or along with antiretroviral therapy (ART), to achieve better outcomes. In view of the high prevalence, morbidity and mortality in this group of individuals in the South-East Asia Region, a comprehensive surveillance, diagnosis and management strategy integrated with HIV programmes needs to be established.

## 2.4 Hepatitis E

Hepatitis E was not recognized as a distinct human disease until 1980 (111–113). Hepatitis E is caused by infection with the hepatitis E virus (HEV), a non-enveloped, positive-sense, single-stranded RNA virus (114–116). Four genotypes 1, 2, 3 and 4 HEV, have been recognized (117). Each HEV genotype appears to have a specific geographic distribution. Genotype 1 HEV has been isolated from human cases of epidemic and sporadic hepatitis E in parts of Asia and Africa, where the disease is highly endemic. Genotype 2 sequences, first reported from an outbreak of hepatitis E in Mexico, have subsequently been reported from cases in western Africa (118, 119). Genotype 3 HEV, first identified in a few rare cases of locally acquired hepatitis E in the United States of America (USA) has subsequently been reported from human cases in several

industrialized countries in Europe, as well as in Asia-Pacific (120–122). Genotype 4 HEV has been found in sporadic cases with acute hepatitis from China, Japan, Taiwan and Viet Nam (123). All genotypes share at least one major serologically cross-reactive epitope and belong to a single serotype (124). Genotype 3 and 4 isolates of HEV appear to be somewhat less pathogenic in humans than those from genotypes 1 and 2. Although the human is considered as the natural host for HEV, antibodies to HEV or closely related viruses have been detected in primates and several other animal species (125–129).

Outbreaks of HEV infection of up to several hundred to several thousand persons have been reported frequently in the Indian subcontinent, China, south-east and central Asia, the Middle East, and northern and western parts of Africa (130, 131). Hepatitis E outbreaks are characteristically associated with a high disease attack rate among pregnant women. Further, affected pregnant women are more likely to develop fulminant hepatitis (131–134). In high-endemic countries, sporadic cases of HEV infection are very common (135–137).

In many high-income countries of America, Asia-Pacific and Europe, hepatitis E is responsible for only occasional cases of acute viral hepatitis. Initially, most such cases were found to be related to travel to high-endemic areas. However, in recent years, solitary cases or small case-series related to autochthonous (locally acquired) hepatitis E in these Regions have been reported. There is well-documented evidence of foodborne transmission of HEV after consumption of uncooked or undercooked pig liver or the meat products of domestic or wild animals (138–147).

In Member States of the WHO South-East Asia Region, annual symptomatic cases of hepatitis E are estimated at 12 million, with 42 000 deaths and 1800 stillbirths. More than 50% of global deaths from hepatitis E occur in the Region (148).

Hepatitis E outbreaks have been documented in all countries of the Region, except the Democratic People's Republic of Korea. Most outbreaks of hepatitis E are related to consumption of faecally contaminated drinking water, and may affect several hundred to several thousand people. Some outbreaks have occurred in urban areas with leaky water pipes contaminated with sewage. Intermittent water supply in these areas leads to a negative pressure in pipes during periods of no flow, permitting inward suction of contaminants (132, 149–156).

In comparison, only a few foodborne outbreaks have been reported. This may be due partly to the difficulty of relating consumption of a particular food to the occurrence of a disease with a relatively long incubation period. Overall attack rates during hepatitis

E outbreaks have ranged from 1% to 15%. Disease rates are the highest among young adults. The lower disease rates seen in children are probably due to a higher proportion of asymptomatic infections in children, rather than to a lower frequency of infection. Hepatitis E cases in males often outnumber those in females. Hepatitis E outbreaks are characteristically associated with a high disease attack rate among pregnant women. Further, the affected pregnant women are more likely to develop fulminant hepatitis (15–22%) or to have a fatal outcome. Fulminant hepatitis E infection has been reported among 40.3% of pregnant women who were coinfectd with chronic hepatitis B (157–159). Hepatitis E during pregnancy is also associated with prematurity, low birth weight and an increased risk of perinatal mortality (148).

In addition to outbreaks, HEV infection accounts for a large proportion of acute sporadic hepatitis infection in all age groups. For example, in a group of patients with sporadic hepatitis E infection, resembling those of an epidemic of hepatitis E in age distribution, severity and duration of illness, pregnant women have a propensity for worse prognosis. It is well documented that HEV superinfection can occur in patients with pre-existing chronic liver disease of viral or non-viral etiology, leading to superimposed acute liver injury and clinical presentation with acute or chronic liver disease. In some patients, chronic liver disease had been clinically silent until the time of HEV superinfection (138).

Comparative studies carried out in Bangladesh, India, Indonesia, Nepal and Thailand have demonstrated that 38–68% of all acute hepatitis has been associated with HEV infection (1, 157, 158).

Interest in hepatitis E has increased significantly in the last few years, owing to the realization that HEV infection may be geographically more widespread than was previously believed, and the number of papers published annually in peer-reviewed journals on this subject has doubled in last five years(132). However, there is a lack of solid surveillance data on hepatitis E infection, owing to the absence of routine reporting and laboratory investigation of suspected hepatitis E cases and outbreaks. In addition, currently available laboratory diagnostic kits for hepatitis E produced by different institutions are not standardized, and a panel of referral sera samples for quality control has not been developed.

Updated estimates of the global burden of disease due to HEV must be generated, based on seroprevalence studies and case-series, to estimate the case-fatality rate. This information is crucial for evidence-based recommendations for the prioritization of further development of hepatitis E vaccine, as well as for determining strategies for

HEV control. The increase in research activity expected in the next few years may lead to development of prevention of HEV infection and strategies for the use of HEV vaccines. Currently, two experimental hepatitis E vaccines are available, which have been demonstrated as safe and highly effective (161–163). However, their effective application requires more detailed population-based studies to assess and estimate the burden of disease caused by HEV infection. Finally, before the vaccine is introduced widely, major emphasis should be placed on the improvement of hygienic and sanitary conditions in countries in the Region, with provision of safe water and promotion of good personal hygiene.

## 2.5 The burden of viral hepatitis

Based on a careful analysis of data on viral hepatitis presented in various national and international symposia, international scientific journals and magazines and WHO documents and publications, the following estimates have been formulated for the current regional burden of viral hepatitis in the South-East Asia Region:

- Hepatitis A: 400 000 cases with 800 deaths annually;
- Hepatitis B\*: 1 380 000 cases with 300 000 deaths annually;
- Hepatitis C\*: 500 000 cases with 120 000 deaths annually;
- Hepatitis E: 12 million cases with 42 000 deaths and 1800 stillbirths annually;
- Acute hepatitis of unknown etiology: 200 000 cases with 5000 deaths.

\*Includes cirrhosis and liver cancer.

In summary, more than 14 million cases of viral hepatitis, with more than 420 000 deaths, occur annually in the WHO South-East Asia Region. In addition to the loss of more than 0.4 million lives and untold suffering for millions of people, viral hepatitis causes tremendous economic loss to the patients and their families, owing to long hospitalization and management of complications, particularly in chronic patients.

Although chronic HBV and HCV infections are among the leading causes of preventable deaths in countries of the South-East Asia Region, about 60% of infected individuals are unaware of their infection status until they become symptomatic with liver cancer or liver disease. Among high-risk populations, rates of testing for hepatitis infection, or even of receiving information on reducing the risk of infection, are very low.

Groups at high risk for hepatitis B virus infection are infants born to women with the disease, sexual contacts of infected persons, and injecting drug users. Persons at highest risk for HCV infection are those who have received a blood transfusion, and past or current injecting drug users, with a prevalence approaching 90% among long-term users. Mortality from hepatitis C is increasing and is greatest among middle-aged men.

Further compounding the problem of undiagnosed hepatitis B and C infection is the generally low level of knowledge about these infections among health-care workers and social service providers. Many providers do not comply with WHO and national guidelines and recommendations for hepatitis B and C screening, prevention, treatment and follow-up services.

Despite the significant public health burden posed by hepatitis B and C, current resources and efforts to curb this problem are inadequate for prevention, control, and surveillance programmes for chronic viral hepatitis, and are notably less than those targeting other infectious diseases that have a similar impact on public health. These discrepancies are particularly striking in light of the observation that there are an estimated 100 million hepatitis B carriers and nearly 30 million hepatitis C carriers, compared to 3.5 million people living with HIV/AIDS in the South-East Asia Region (see Table 4). In other words, the estimated number of hepatitis B and hepatitis C carriers is 28 times and 8 times higher than the estimated number of people with HIV/AIDS in the Region, respectively.

Table 4: Estimated number of hepatitis B, hepatitis C and HIV infections in the WHO South-East Asia Region

Countries of the WHO South-East Asia Region	Population <sup>a</sup> (millions)	Estimated HBsAg carriers <sup>b</sup>		Estimated HCV carriers <sup>c</sup>		Estimated HIV carriers <sup>c</sup>	
		Number (millions)	%	Number (millions)	%	Number (millions)	%
Total	1784	100	5.6	29.1	1.62	3.51	0.2

<sup>a</sup> Population data from World Health Statistics 2011, WHO.

<sup>b</sup> Data from various sources (government report, scientific publications).

<sup>c</sup> Data from HIV/AIDS in South-East Asia Region progress report 2010, WHO South-East Asia Regional Office.

The estimated number of deaths related to hepatitis B, hepatitis C, cirrhosis, hepatocellular cancer and selected communicable diseases in the WHO South-East Asia Region, based on data from the WHO *Global burden of disease* 2004 (164) and the update 2008 (165), is presented in Table 5.

Table 5: The estimated number of deaths related to hepatitis B, hepatitis C, cirrhosis, liver cancer and selected communicable diseases in the WHO South-East Asia Region

Disease	Estimated number of deaths	
	2004 (164)	2008 (165)
Hepatitis A	Not included in estimation	Not included in estimation
Hepatitis B	37 017	53 145
Hepatitis C	13 686	19 996
Hepatitis E	Not included in estimation	Not included in estimation
Cirrhosis	210 160	284 292
Liver cancer	58 452	62 491
Dengue	10 627	8690
Malaria	36 498	19 996
HIV/AIDS	206 086	244 277
Tuberculosis	518 717	490 194

Approximately 70–80% of cases of cirrhosis and liver cancer are associated with hepatitis B and hepatitis C infections (17, 166). The information presented in Table 5 is noteworthy in that the estimated number of deaths in the Region associated with viral hepatitis and its consequences (cirrhosis and liver cancer) is much higher than the estimated number of deaths caused by malaria, dengue and HIV/AIDS combined. This estimation does not include deaths associated with hepatitis A and hepatitis E. Deaths associated with viral hepatitis are highest for all communicable diseases except tuberculosis (TB) (164,165).

## 2.6 Issues that need to be addressed

A review of available data reveals that infection with various hepatitis viruses, A–E, is common in the WHO South-East Asia Region.

Among enterically transmitted viruses, seroprevalence rates for hepatitis A virus are high in most countries in the Region, but with a recent decline. The consequent increase in average age at first exposure has led to an increase in the number of clinical



cases of hepatitis A, including severe forms of disease. A vaccine against hepatitis A is available but it is not yet being used as a public health measure in the Region; further, its utility in the South-East Asia Region remains to be determined. Infection with hepatitis E virus is highly endemic in several countries, and causes frequent waterborne outbreaks and nearly half of all cases of acute viral hepatitis in many countries.

Among bloodborne hepatitis viruses, hepatitis B virus infection rates vary between low: <2% (1, 9–11), intermediate: 2–8% (13–16, 18–33) and high: >8% (34–42) among various countries in the Region. Hepatitis C virus infection rates in the Region vary from 1% to 3%. Infection with either of these viruses can be persistent, lead to development of cirrhosis and liver cancer, and account for a large number of deaths. These infections are more common in some specific population groups, e.g. intravenous drug users, recipients of blood transfusions, certain occupational groups such as health-care workers, and immunosuppressed persons (including those with HIV infection). Hepatitis B vaccine is part of national immunization programmes in all countries in the South-East Asia Region; however, the current coverage rates are low in some areas and vaccination at birth has not been universally adopted. Also, screening of blood and blood products for agents causing viral hepatitis is inadequate in some areas.

Thus, infection with hepatitis viruses causes a significant disease burden in the South-East Asia Region, in the form of both acute and chronic hepatitis. However, the available data from the Region on rates of infection with hepatitis viruses, rates of clinical disease caused by these viruses, and the associated morbidity and mortality are limited and may not provide a complete picture. Further, there are no data on the societal and economic impact (in terms of years of life lost, disability, loss of productivity, expenditure on medical care, etc.) of these infections in the Region.

The problems associated with viral hepatitis in the Region include:

- low levels of awareness among health administrators and policy-makers, medical professionals and the general population about hepatitis viruses, including their routes of transmission, risk factors and impact on human health;
- inadequate disease surveillance systems, with a high likelihood of underreporting of both acute and chronic infections, leading to insufficient understanding of the magnitude and seriousness of the public health problems associated with viral hepatitis;

- limited knowledge, availability of, access to and use of preventive services for viral hepatitis, including screening of transfused blood and blood products;
- rapid urbanization, overpopulated cities and lack of access to clean water and sanitation;
- limited testing facilities for detection of chronic HBV or HCV infection, leading to a large proportion of persons with chronic infection remaining undiagnosed;
- the high cost of and inadequate access to treatment for viral hepatitis and for its long-term complications (cirrhosis and liver cancer) and liver transplantation in patients with end-stage disease;
- inadequate financial and manpower resource allocation and public spending on programmes for surveillance, prevention and control of viral hepatitis, leading to insufficient understanding of the extent and seriousness of this public health problem;
- low rates of infant hepatitis B vaccine coverage, particularly for the dose at birth, in some parts of the Region.

All these issues have been considered during finalization of the strategy for the prevention and control of viral hepatitis in the South-East Asia Region.

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## 3. The vision, goal, mission, structure and implementation of the strategy

### 3.1 Vision

The vision of the *Regional strategy for the prevention and control of viral hepatitis* is that the public health and clinical impact of infection with hepatitis viruses in the South-East Asia Region is reduced to a minimum.

### 3.2 Goal

The goal of the strategy is implementation of policies, programmes and interventions to interrupt transmission and reduce the incidence and socioeconomic consequences of viral hepatitis in the countries of the South-East Asia Region.

### 3.3 Mission

The mission of this strategy is to outline a coordinated, comprehensive and systematic approach that will decrease the incidence of viral hepatitis and reduce the associated morbidity and mortality.

### 3.4 Structure

The *Regional strategy for the prevention and control of viral hepatitis* is organized by the following six topic areas/pillars, which correspond to the needs and recommendations

for prevention and control of viral hepatitis in the Member States of the WHO South-East Asia Region:

- (1) strategic framework for policy, planning, advocacy and resource mobilization;
- (2) strategic framework for surveillance;
- (3) strategic framework for research;
- (4) strategic framework for prevention and control;
- (5) strategic framework for education;
- (6) strategic framework for medical care and treatment.

For each topic area/pillar, the regional strategy offers a dedicated chapter that begins with background information and is followed by recommended goals, strategies and actions to be undertaken by all stakeholders involved in the prevention and control of viral hepatitis in the Member States of the WHO South-East Asia Region. Recommended actions are listed by calendar year of initiation.

These regional strategic pillars/frameworks are aligned with the four strategic axes of WHO's global comprehensive approach for the *Prevention and control of viral hepatitis infection* (1) (see Table 6).

Table 6: Comparison of WHO's strategic axis and the South-East Asia Region Strategic Frameworks

WHO's strategic axis (1)	Regional strategic framework
1. Partnership, mobilization and communication	1. Policy, planning, advocacy and resource mobilization (building the infrastructure for sound policy and programme development)
2. Data for policy and action	2. Surveillance 3. Research for improvement of the viral hepatitis prevention and control programmes
3. Prevention of transmission	4. Prevention (promoting risk reduction, safe health care, screening blood and blood products, safe medical manipulations/injections and hepatitis B virus vaccination) 5. Education (improved knowledge and awareness)
4. Screening, care and treatment	6. Medical care and treatment (assuring timely access to care, treatment and other related services for patients with acute and chronic viral hepatitis)

## 3.5 Implementation

The regional strategy defines actions that need to be undertaken by countries, with support from WHO. Successful implementation of this strategy requires leveraging multiple opportunities. Some of the actions can be accomplished through improved coordination and integration of existing activities, whereas others are subject to the availability of funds. Also critical to the overall success of this plan are policy-related support and system changes, which are highlighted in the other WHO and national documents related to the improvement of public health, primary health care, the national HIV/AIDS strategy, the national prevention and health promotion strategy, the national vaccination strategy, and prevention and control of health-care associated infections. Components of each of these initiatives are reflected in the Viral hepatitis action plan, resulting in a multifaceted, comprehensive approach to preventing viral hepatitis and improving the lives of millions of infected persons.

Within a reformed health-care system, the Regional strategy for the prevention and control of viral hepatitis will offer an unprecedented opportunity to provide people, particularly those in vulnerable and underserved populations, with improved services for prevention, care and treatment of viral hepatitis.

The implementation of the *Regional strategy for the prevention and control of viral hepatitis* should be reviewed in 2015 and modified based on needs.

## 3.6 Reference

- (1) Prevention and control of viral hepatitis infection: framework for global action. Geneva: World Health Organization; 2012 (WHO/HSE/PED/HIP/GHP 2012.1, [http://www.who.int/csr/disease/hepatitis/GHP\\_Framework\\_En.pdf](http://www.who.int/csr/disease/hepatitis/GHP_Framework_En.pdf), accessed 16 October 2013).



## 4. Strategic framework for policy, planning, advocacy and resource mobilization

	Hepatitis A ,B C and E
Goal	Foster an effective policy, planning, advocacy and resource mobilization environment for prevention and control of viral hepatitis at the national and regional levels
Strategies	<p>Create an adequate statutory and regulatory environment for prevention and control of viral hepatitis</p> <p>The regional technical advisory group on viral hepatitis should base policy development decisions on credible information</p> <p>Provide policy-makers with information on the impact of challenges and unmet needs related to viral hepatitis</p> <p>Advocate and organize resource mobilization for prevention and control of viral hepatitis</p>

The framework for policy, planning, advocacy and resource mobilization is identified as a priority issue in the prevention and control of viral hepatitis for the following reasons:

- currently there is no formal comprehensive policy to support control of viral hepatitis in the Region;
- the focal person or institution identified by the ministry of health as a coordinator for control of viral hepatitis has multiple competing responsibilities that leave a minimal amount of time to focus on planning, advocacy and funding initiatives;
- organizations/institutions that have a similar mission (namely HIV) do not focus on viral hepatitis B and C;

- there is an absence of an open forum for sharing technical information on prevention and control of viral hepatitis;
- funding for viral hepatitis at the national and regional levels has been scarce; it is essential to continue advocating for, identifying and securing consistent sources of funding to expand prevention and control of viral hepatitis in the countries of the WHO South-East Asia Region;
- there is significant stigma associated with viral hepatitis in many countries and those infected often suffer discrimination. Special programmes need to be designed to reduce stigma and eliminate discrimination.

## 4.1 Policy and planning

### Strategy – create an adequate statutory and regulatory environment for prevention and control of viral hepatitis

As follow-up to the World Health Assembly resolution WHA63.18 (1), which refers to the need for a comprehensive approach to the prevention and control of viral hepatitis, Dr Samlee Plianbangchang, Regional Director of the WHO South-East Asia Region, made a statement on World Hepatitis Day, 28 July 2011, that viral hepatitis must be given greater priority in terms of both resources and efforts in all Member States of the WHO South-East Asia Region. Further to the Regional Director's directives and recommendations, a focal point in the Regional Office for South-East Asia, responsible for the coordination of work in the field of prevention and control of viral hepatitis, should be nominated. The focal point for viral hepatitis is the contact person to whom any issues related to the viral hepatitis prevention and control programme should be addressed, who is particularly responsible for coordination, identification of needs and development of funding proposals for the South-East Asia Region.

The work of the focal point will be supported by a "viral hepatitis working group". This group, at the Regional Office for South-East Asia, will include representatives from all relevant technical units and will meet on a regular basis, depending on needs, or at least every 6 months. Viral hepatitis focal points will also be nominated in WHO country offices, who will be responsible for overseeing viral hepatitis programmes at the country level. The Regional Office for South-East Asia will be responsible for providing technical briefing and the latest technical information to the WHO country offices, on the prevention and control of viral hepatitis.

All members of the WHO South-East Asia Region consider viral hepatitis as an urgent public health issue. However, in the majority of the countries of the Region, activities related to surveillance, prevention and control, and treatment of viral hepatitis are integrated as part of various health programmes, under the responsibility of various authorities. There are no specially defined offices, persons or programmes for integrated coordination and support of viral hepatitis activities and services, either by the ministry of public health or by professional associations.

In Thailand, previously, a national committee on viral hepatitis was set up to provide recommendations to the ministry of public health on policy for prevention and control of viral hepatitis. This committee was of an ad hoc nature, but contributed significantly to the initiation of hepatitis B vaccination policy. Currently only the Democratic People's Republic of Korea and Indonesia have units in the ministry of health responsible for the prevention and control of viral hepatitis. In the Democratic People's Republic of Korea, the National Hepatitis Research Center supports policy development and strategy implementation. The ministry of health in Indonesia has formed a national committee on viral hepatitis, consisting of 16 members. The members of the committee are from major universities and national health research institutions and major hospitals. The main task of this committee is to technically support the ministry of health in the formulation and implementation of the viral hepatitis prevention and control programme.

To improve the existing programmes for prevention and control of viral hepatitis in Member States of the Region, the following recommendations are suggested:

- identify a focal person or establish a unit in the ministry of health responsible for the coordination of prevention and control of viral hepatitis;
- establish a national committee on viral hepatitis; this committee should be responsible for the development of a national strategy and programmes for the prevention and control of viral hepatitis, and its supervision, coordination, implementation and monitoring at the national level;
- the committee would consist of persons representing all agencies that will play an active role in the viral hepatitis programme; these individuals should be occupying executive positions in their respective departments;
- the coordinator or chairman of this committee would be a high-ranking official with the power to coordinate and supervise representatives from different divisions/units and institutions involved in the viral hepatitis programme;

- the suggested composition of the national committee is:
  - chairman – a high-ranking government official;
  - secretary of the committee – the person/unit in the ministry of health responsible for the coordination of viral hepatitis;
  - representatives of units responsible for surveillance, laboratory diagnosis, blood safety, case-management and treatment;
  - staff of leading institutions and hospitals working in the field of viral hepatitis;
  - staff of major NGOs involved in a viral hepatitis programme;
  - representatives of patients with viral hepatitis;
  - WHO technical staff from the WHO country office;
  - representative(s) of the media.

The national committee should meet every 6 months and should nominate one or two members to be part of the WHO South-East Asia Region technical working group for viral hepatitis.

### **Actions to be initiated during 2013**

- Establish a viral hepatitis working group at WHO Regional Office for South-East Asia and identify technical staff in WHO country offices responsible for viral hepatitis at country level
- Further carry out implementation of the WHA63.18 resolution (1) in the South-Asia Region
- Member States should engage in technical discussions on the prevention and control of viral hepatitis
- Member States should consider establishing/strengthening a unit in the ministry of health responsible for the coordination of prevention and control of viral hepatitis, and establishing a national committee on viral hepatitis

### **Actions to be initiated during 2015**

- Review the implementation of the strategic framework for policy, planning, advocacy and resource mobilization

## **Strategy – the regional technical advisory group on viral hepatitis should base policy development decisions on credible information**

In order to adequately support efforts of Member States and the WHO Regional Office for South-East Asia for the prevention and control of viral hepatitis, the informal consultation meeting suggested formation of a regional technical advisory group on viral hepatitis, comprising eminent scientists, public health professionals and decision-makers working in this field. The advisory group would oversee implementation of the *Regional strategy for prevention and control of viral hepatitis* in the Region, and advise on any necessary revisions and changes, if required. The following terms of reference for the RTAG on viral hepatitis are proposed:

- to advise the Regional Director on policies, strategies and activities that are crucial for the prevention and control of viral hepatitis in the Region;
- to provide strategic direction in implementing the *Regional strategy for prevention and control of viral hepatitis* in Member States;
- to identify the strengths and weaknesses of the control strategy and make practical recommendations;
- to advise on the use of appropriate and new technologies for effective prevention and control of viral hepatitis;
- to identify areas of research and capacity-building required by countries.

### **Actions to be initiated during 2013**

- The regional technical advisory group on viral hepatitis to be formed

### **Actions to be initiated during 2014**

- First meeting of the regional technical advisory group to be conducted

## **4.2 Communication for advocacy**

### **Strategy – provide policy-makers with information on the impact of challenges and unmet needs related to viral hepatitis**

Advocacy is urgently needed to create awareness among policy- and decision-makers regarding the importance and impact of viral hepatitis. National meetings, symposiums and other forums on public health should be appropriately used for the promotion of

prevention and control of viral hepatitis. Particular attention should be given to the preparation of advocacy documents, which should contain useful information that can easily be accessed by politicians, administrators and community leaders.

It is important to have close collaboration with the media, to expand and improve the quality of coverage of viral hepatitis programmes. Clear, consistent and strong media messages for all audiences should be developed and delivered. Personal stories should be used in mainstream media, to counter fear and discrimination, and build empathy and understanding. A viral hepatitis journalism award should be established, to improve the quantity, quality and regularity of reporting. Information should be provided to the media on preferred terminology and language.

It is important to build strong relationships with decision-makers and leaders, to encourage effective action and ensure the interests of people with viral hepatitis are heard and addressed. It is crucial to provide short messages to high-level political leaders; the need for and shortage of resources should be highlighted. Information regarding the mortality, morbidity and economic losses associated with viral hepatitis should be disseminated. Meetings should be organized with eminent scientists in the field of viral hepatitis, as well as political leaders, parliamentarians and the business community. Parliamentarians should be invited to a technical meeting to help them better understand how serious the viral hepatitis problem is. Regular information on the needs, progress and achievements of the national and regional programmes for prevention and control of viral hepatitis should be provided to the government and national and international funding agencies.

The third important component of this strategy is to connect different organizations and groups for advocacy of prevention and control of viral hepatitis. Meetings and seminars organized by United Nations agencies should be used to advocate prevention and control of viral hepatitis. NGOs working in the field of viral hepatitis should be promoted and opportunities provided for people affected by viral hepatitis to speak on their own behalf at decision-making meetings.

In addition, there is a need to develop an open forum for sharing technical information on prevention and control of viral hepatitis among the Member States of the Region.

### **Actions to be initiated during 2013**

- Formulate a regional and national plan of work with media regarding viral hepatitis

### **Actions to be initiated during 2014–2015**

- Develop standard information kits on viral hepatitis for countries in the Region, including the decision-makers and leaders

## **4.3 Resource mobilization**

### **Strategy – advocate and organize resource mobilization for prevention and control of viral hepatitis**

One of the major constraints is limited resources allocated for prevention and control of viral hepatitis in the countries of the Region. There is an urgent need to generate resources for surveillance and laboratory diagnosis of viral hepatitis, hepatitis B vaccine and conducting an immunization campaign, and for treatment and care of acute HAV and HEV and chronic HBV and HCV infections. The health-care cost, especially the cost of treatment for chronic HBV and HCV, is very high and varies from country to country.

Member States of the WHO South-East Asia Region need to work together to mobilize resources. Based on an analysis of the current situation, the following actions are suggested:

- develop a strategy for resource mobilization and a list of priorities for funding;
- identify potential proposal writers for funding purposes;
- identify potential financial institutions interested in providing resources for the prevention and control of viral hepatitis, and involve high-level government officials and dignitaries in the process of fundraising;
- build relationships with national/international business communities and organizations, to provide a forum for raising donations; advocate fundraising for viral hepatitis in various meetings and symposiums.
- regularly update community, government and donor agencies regarding resources that have been received for the viral hepatitis programme and how effectively they have been used;
- organize meetings and seminars with potential donors, for fundraising purposes.

### **Actions to be initiated during 2013**

- Develop the regional and national workplan for resource mobilization for prevention and control of viral hepatitis

### **Actions to be initiated during 2014**

- Conduct a fundraising meeting for viral hepatitis programmes in the Region

## **4.4 Reference**

- (1) Resolution WHA63.18. Viral hepatitis. In: Sixty-third World Health Assembly, Geneva, 17–21 May 2010. Geneva: World Health Organization; 2010 (A63/15, [http://apps.who.int/gb/ebwha/pdf\\_files/WHA63/A63\\_15-en.pdf](http://apps.who.int/gb/ebwha/pdf_files/WHA63/A63_15-en.pdf), accessed 16 October 2013).



# 5. Strategic framework for surveillance

	Hepatitis A , B, C and E
Goal	Foster an effective policy, planning and resource mobilization environment for viral hepatitis surveillance at the national and regional levels
Strategies	<div>Establish an effective surveillance system for viral hepatitis and improved capacity for complete and accurate disease reporting</div> <div>Standardize data collection systems for the core and targeted surveillance for viral hepatitis</div> <div>Improve the epidemiologic investigation and response capacity to outbreaks</div> <div>Identify, or develop and evaluate, evidence-based interventions for prevention and control of viral hepatitis</div>

Public health surveillance is defined as ongoing systematic collection, analysis and interpretation of health data essential for planning, implementing and evaluating public health activities, closely integrated with timely dissemination of data to enable effective and efficient action to be taken to prevent and control diseases.

The role of surveillance for viral hepatitis has been determined in the following waysaz:

- (1) identifying acute outbreaks of hepatitis A, B, C and E virus infections and individual acute cases and measuring their incidence, responding to outbreaks by:
- identifying cases;

mobilizing appropriate resources to provide preventive services to eliminate or minimize further transmission;

developing accurate estimates of the burden of acute cases of hepatitis A, B, C and E infection;

- (2) identifying chronic cases of hepatitis B and C and measuring their prevalence:
  - developing accurate estimates of the burden of chronic hepatitis disease;
  - preventing secondary cases;
  - hepatitis B – education, vaccination and screening;
  - hepatitis C – education, harm reduction and screening;
- (3) linking cases to appropriate services, including medical management of infected persons;
- (4) evaluating current practices and prevention efforts.

Information regarding the use of surveillance data, outbreak detection, clinical description, laboratory criteria for diagnosis and case classification is presented in *Annex 2*.

## 5.1 Challenges for viral hepatitis surveillance systems

Many of the people affected by viral hepatitis have limited access to health care (for example, people living in poverty, active injecting drug users and marginalized populations) and are less likely to be diagnosed appropriately to provide complete and accurate demographic and behavioural information, or to access follow-up care. Each HBV-infected or HCV-infected person who does not enter into appropriate medical care represents a missed opportunity for secondary prevention and may contribute to the collection of inaccurate and less detailed surveillance data. Finding ways to ensure that patients receive comprehensive and culturally appropriate care and referrals not only would increase the likelihood of improving their health outcomes, but is likely to favourably affect collection of surveillance data.

### **Strategy – establish an effective surveillance system for viral hepatitis and improved capacity for complete and accurate disease reporting**

Current public health surveillance systems for viral hepatitis can be significantly improved. As a result, either surveillance data do not provide accurate estimates of the current burden of disease or they are insufficient for programme planning and evaluation, and do not provide information that would allow policy-makers to allocate sufficient resources to address the problem.

As a result, information is incomplete, variable and inaccurate. Inconsistency between surveillance in different areas undermines the validity of data provided at national and regional levels. The inability of health-care providers to track all diagnosed cases also undermines case-management and prevention efforts.

There is limited published information on, or systematic review of, surveillance of viral hepatitis in the countries of the WHO South-East Asia Region. In contrast, the history and status of national HIV surveillance is well reviewed and documented in almost all countries of this Region. A comprehensive review of viral hepatitis surveillance is therefore needed, in order to document current systems and capacities of public health jurisdictions. The evaluation should focus on developing guidelines to improve the consistency of surveillance data and should provide guidance on the development of detailed technical guidelines and standards for hepatitis surveillance programmes. There is a need to establish or nominate an institution able to serve each country as a national referral centre for surveillance, prevention and control of viral hepatitis. This institution should be responsible for reviewing current surveillance of viral hepatitis and lead the integration of viral hepatitis surveillance with other disease surveillance systems. It should also be responsible for coordinating and providing guidance to all health institutions in the country, regarding surveillance, prevention and control of viral hepatitis.

A successful surveillance system for viral hepatitis requires standardized laboratory procedures, standard diagnostic kits and a standard reporting system. It is well known that automated electronic laboratory reporting improves the completeness and timeliness of disease surveillance and this should be used for surveillance of viral hepatitis. It is important that, based on the technical expertise and resources that are available, an institution is established or nominated that is able to serve the country as a referral centre for laboratory diagnoses of viral hepatitis. This institution should be responsible for monitoring quality control of laboratory diagnoses of viral hepatitis, as well as conducting prequalification of diagnostics used in the country. The aim of the prequalification of the diagnostics programme should be to promote and facilitate access to safe, appropriate and affordable diagnostics of good quality, in an equitable manner. The focus should be on diagnostics for high-burden diseases and their suitability for use in resource-limited settings. To carry out prequalification of viral hepatitis diagnostics, standard procedures as described in the recent WHO document *Overview of the prequalification of diagnostics assessment process. Prequalification of diagnostics (1)* should be followed. WHO should facilitate and technically support this process.

### **Actions to be initiated during 2013–2014**

- Review existing disease surveillance systems and conduct a situation analysis to estimate viral hepatitis burden
- Establish/nominate an institution able to serve as a national referral centre for viral hepatitis surveillance, prevention and control (RC-VHSPC), and develop terms of reference for the RC-VHSPC
- Establish/nominate an institution able to serve the country as a referral centre for viral hepatitis laboratory diagnosis (RC-VHLD), and develop terms of reference for the RC-VHLD

### **Actions to be initiated during 2014–2015**

- Viral hepatitis surveillance to be integrated in the other disease surveillance systems
- Viral hepatitis surveillance work to be coordinated and monitored by the RC-VHSPC
- Viral hepatitis laboratory support to be coordinated and monitored by the RC-VHDL
- First regional meeting of RC-VHSPC and RC RC-VHLD planned in 2014–2015
- Prequalified diagnostics to be used for laboratory diagnoses for viral hepatitis
- Plan of work to be developed for 2015–2016 for RC-VHSPC and RC-VHLD

## **5.2 Model for viral hepatitis surveillance**

### **Strategy – standardize data collection systems for the core and targeted surveillance for viral hepatitis**

To analyse data on surveillance for viral hepatitis in the countries of the Region, the regional consultation meeting recommended surveillance based on the development of a model designed to improve the quality and accuracy of information, and development of systems to collect, analyse and disseminate data on acute HAV and HEV infections and acute and chronic HBV and HCV infections.

These recommendations call for a two-part system (see Figure 3):

- (1) core surveillance activities, building the capacity at the national level to conduct standard disease surveillance on diagnosed acute HAV and HEV infections and acute and chronic HBV and HCV infections;
- (2) targeted surveillance, to obtain data on specific populations that are not represented fully in the collection of core surveillance data.

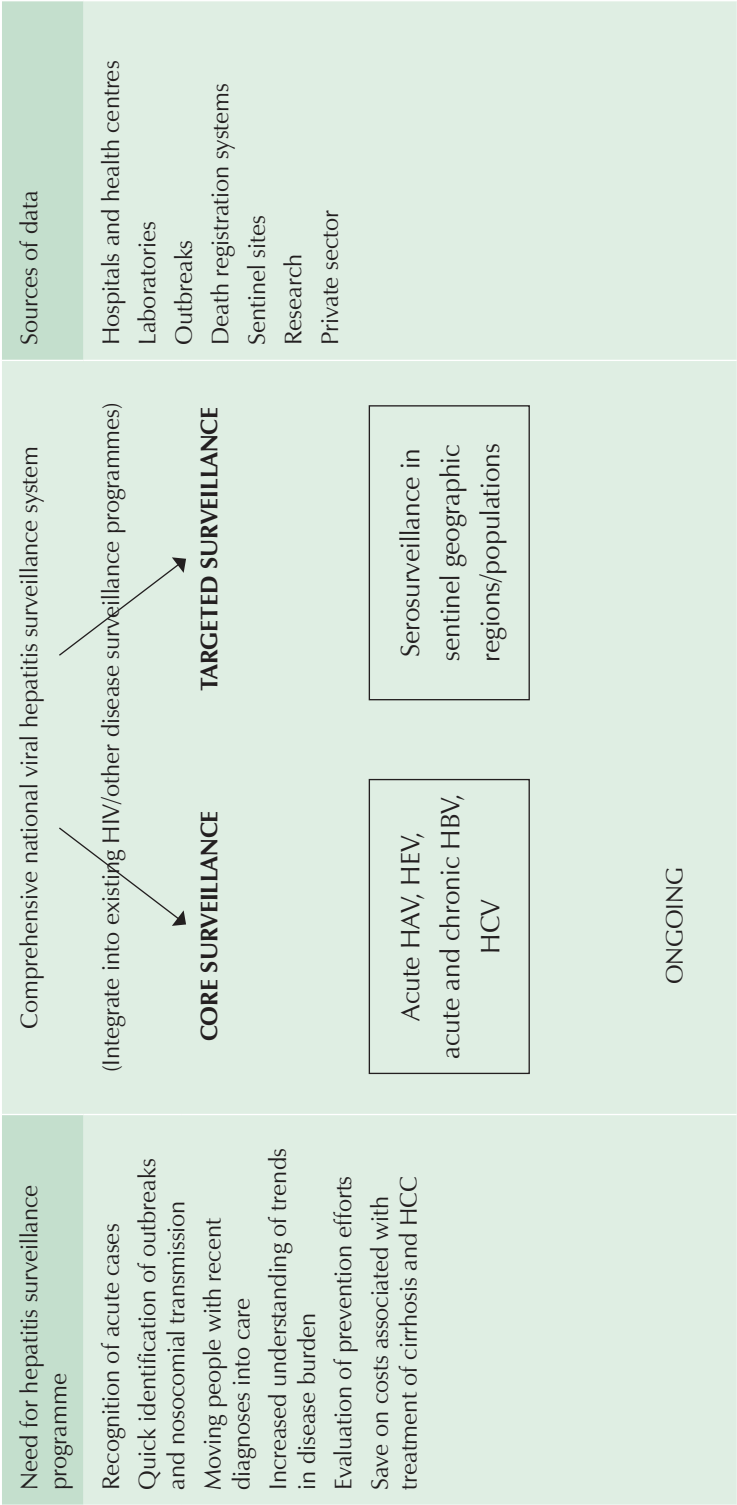
Core surveillance means those activities in which all jurisdictions must engage to provide accurate, complete and timely information to monitor incidence, prevalence and trends in disease diagnoses. Data from other activities, such as targeted surveillance, supplement information from core surveillance that is necessary to provide accurate incidence estimates, given the challenges of conducting surveillance for viral hepatitis.

The initial focus of the programme should be the development and implementation of standardized systems to maximize their capacity to perform core surveillance for acute and chronic viral hepatitis infection. Standardization will be accomplished through improved guidance and adequate and consistent funding. Systems should be integrated into existing HIV or other disease surveillance infrastructure, where feasible. Complementary efforts need to be made in building enhanced supplemental surveillance systems to describe trends in underrepresented at-risk populations better and to address the gaps identified in the current surveillance system. Both types of surveillance activities will provide better information to policy-makers and service-delivery systems, to improve care for people who are at risk or are living with HBV or HCV infection. Changes should be phased and prioritized, with the first step focused on the development and funding of core surveillance systems for each country.

## Core surveillance

Core surveillance, including collection, processing, analysis and dissemination of data on cases of acute HAV and HEV infection and acute and chronic HBV and HCV infection, is needed. Because of the public health importance of quick identification of outbreaks and nosocomial transmission, acute disease surveillance has had the highest priority in surveillance programmes in the past. However, chronic disease surveillance is also critical in that, if funded appropriately, it will assist in the recognition of acute cases, aid in moving people with recent diagnoses into appropriate care, contribute to an increased understanding of disease burden, allow evaluation of prevention efforts, and, given appropriate case-management, save on the costs associated with treatment

Figure 3: National viral hepatitis surveillance



of patients who have cirrhosis and HCC. Proper chronic disease surveillance can also improve acute disease surveillance, by enhancing the accuracy and efficiency of related data collection. Evaluation of the core surveillance system should be ongoing, to ensure that it is meeting emerging needs.

## **Targeted surveillance**

Once core hepatitis B and hepatitis C surveillance activities are well established, supplemental or pilot projects should be tested. It is suggested by the technical advisory group on viral hepatitis to develop and support innovative supplemental surveillance programmes. Active surveillance should be conducted in specific (sentinel) geographical regions and populations. Supplemental surveillance projects should include serosurveillance among targeted populations. Serosurveillance projects will provide data for improved estimation of the scope of the problem in underrepresented and at-risk populations. For HAV and HEV infection, age-based serosurveillance of the general population is probably more appropriate. Testing for HBV and HCV in at-risk groups with high prevalence is probably more cost effective than mass screening.

### **Actions to be initiated during 2013**

- Work for the development of standard protocols for the core and targeted surveillance of acute HAV and HEV and acute and chronic HBV and HCV

### **Actions to be initiated during 2014–2015**

- New standard protocols for the core and targeted surveillance to be field-tested
- New standard protocols for core and targeted surveillance to be finalized
- RC-VHSPC and RC-VHLD to jointly conduct national training on new standard protocols for surveillance of viral hepatitis

### **Actions to be initiated during 2015**

- Implementation of new standard protocols for viral hepatitis to be monitored

## 5.3 Outbreak investigation and control

### Strategy – improve the epidemiologic investigation and response capacity to outbreaks

Member States of the WHO South-East Asia Region should ensure they have sufficient infrastructure to identify and appropriately investigate outbreaks and sporadic cases of viral hepatitis. Consideration needs to be given to identifying funds to hire staff to process laboratory results, enter data and follow up cases of chronic HBV and HCV infections.

#### Actions to be initiated during 2013

- Review and update current protocols for investigation of viral hepatitis outbreaks

#### Actions to be initiated during 2014–2015

- Updated protocols for investigation of viral hepatitis outbreaks to be disseminated and used

## 5.4 Evidence-based interventions

### Strategy – identify, or develop and evaluate, evidence-based interventions for prevention and control of viral hepatitis

Surveillance data are often used to determine how to use resources most effectively. For example, estimates of disease burden are commonly used to provide guidance to policy-makers on the level of funding required for disease-related programmes. If surveillance data are not available or understate the disease burden, legislators and public health officials will not allocate sufficient resources to mount an appropriate public health response. Information on disease burden is only one factor that guides policy-makers in allocating public health resources. Priorities in public funding are also driven by public awareness and advocacy. Therefore, it is important to communicate surveillance trends and disease burden clearly to policy-makers and community advocates. For example, in countries of the South-East Asia Region, viral hepatitis and its consequences (cirrhosis and liver cancer) are much higher than the number of estimated deaths caused by malaria, dengue and HIV/AIDS combined.



However, despite the large number of individuals and communities affected by viral hepatitis, the resources available for addressing viral hepatitis are only a small fraction of those available for addressing HIV. Looking at the last decade's health development programmes of the countries could easily identify the limited resources that are allocated for viral hepatitis surveillance. Possibly, it was considered that introduction of hepatitis B vaccination under the framework of the EPI is sufficient and resources for surveillance could be reduced. The fact that surveillance data can also be used to evaluate systems for delivery of prevention and care services was ignored.

A key potential role of the hepatitis surveillance programme is to evaluate the effect of HBV vaccination programmes. Unfortunately, this has resulted in a huge gap of information that was needed for advocacy and resource allocation for prevention and control of viral hepatitis. For surveillance of viral hepatitis, linking patients who have recent diagnoses to comprehensive viral hepatitis programmes may be necessary, to ensure access to appropriate services, including clinical evaluation, regular follow-up visits, referral to drug-treatment and harm-reduction programmes, education on liver health, and prevention of transmission to others. WHO should support countries to conduct an evaluation of the national viral hepatitis surveillance system, and a standard protocol should be developed. The evaluation should at least:

- include an assessment of the attributes of the existing surveillance system, including completeness, data quality and accuracy, timeliness, sensitivity, specificity, positive predictive value, representativeness and stability;
- be used to formulate detailed technical guidelines and standards for viral hepatitis surveillance;
- be published in a report.

### **Actions to be initiated during 2013–2014**

- Develop a standard protocol for assessment of viral hepatitis surveillance system
- Conduct an assessment of the viral hepatitis surveillance system in selected countries
- Evaluate the effectiveness of hepatitis B vaccination programmes in selected countries

### **Actions to be initiated during 2014**

- Publish a report the results of assessment of the surveillance system, and the evaluation of the effectiveness of hepatitis B vaccination programmes
- Plan and conduct different components of the viral hepatitis surveillance system evaluation

### **Actions to be initiated during 2015**

- Review the implementation of the strategic framework for surveillance

## **5.5 Reference**

- (1) Overview of the prequalification of diagnostics assessment process. Prequalification of diagnostics. Geneva: World Health organization; 2011 (PQDx\_007 v4; [http://www.who.int/diagnostics\\_laboratory/evaluations/110322\\_pqdx\\_007\\_pq\\_overview\\_document\\_v4.pdf](http://www.who.int/diagnostics_laboratory/evaluations/110322_pqdx_007_pq_overview_document_v4.pdf), accessed 17 October 2013).

# 6. Strategic framework for research

	Hepatitis A , B, C and E
Goal	Determine the interventions required, based on research on prevention and control of viral hepatitis
Strategies	Monitor the changing epidemiological and virological patterns Reduce the risk of transmission Assess the impact of intervention Assess/develop new tools for prevention, diagnosis, care and treatment

Research is used to obtain knowledge on interventions, tools or strategies that enhance programme effectiveness, and is an appropriate method for addressing perplexing questions within public health programmes. Research should be an integral part of any disease control programme. In order to provide reliable answers based on evidence, research should be designed according to sound scientific methods. The need for research as a part of strategic information and an evidence base for developing effective and efficient disease interventions that contribute to scaling up and sustaining interventions that work, cannot be underestimated. In the face of the financial crisis facing countries, priority setting becomes increasingly important, in order to carry out research for health problems that target groups or populations such as the poor, vulnerable, marginalized and underprivileged.

The framework for research on viral hepatitis in this document only identifies the broader areas of research that are currently needed to determine interventions to improve the capacity of the viral hepatitis programme at national and regional levels.

It is important to have a standard methodology and approach to undertake operational research in the field of viral hepatitis. The document *Framework for operations and implementation research in health and disease control programs* (1)

provides information and a checklist of major activities required in the planning, implementation and use of operational research. The priority of areas in research will be changed, based of the needs of the viral hepatitis prevention and control programme.

In 2005, the WHO Regional Office for South-East Asia introduced a Small Grants Programme (SGP), which aims to facilitate and strengthen control-oriented operational research in tropical and communicable diseases in Member States of the South-East Asia Region. The SGP supports research projects by funding, on a competitive basis, research that contribute to the prevention, control and treatment of communicable diseases, including ways of improving the use of existing methods. Only research projects with public health implications and those developed in cooperation with disease control programmes of the ministries of health were eligible for support. Researchers working in the field of viral hepatitis should be encouraged to be involved in the SGP. Top priority will be given to the operational research proposals to improve prevention, surveillance, care and treatment of viral hepatitis. The proposals submitted would be extensively reviewed by the experts, according to their scientific merit, relevance to control activities, and the potential for strengthening operational research capacities. The principal investigators of proposals that meet the above criteria and are selected for funding will be informed. If required, the WHO Regional Office for South-East Asia, in collaboration with international experts, may assist the principal investigators in finalizing their proposals.

The WHO Regional Office for South-East Asia, together with the regional technical advisory group for viral hepatitis, may facilitate the identification of regional and national research priorities for public health, and clinical policies and interventions. It may also undertake advocacy, provide technical justification and identify needs to financial institutions and donor agencies, to obtain resources for research in the field of viral hepatitis. The Regional Office for South-East Asia should also collaborate with Member States and technical partners in building research capacity based on identified need and clear timelines, at national, institutional and individual levels, assist with the design of operational research protocols, and coordinate multicentre studies to address the challenges in viral hepatitis prevention and control programmes in an effective manner. It is important to facilitate national and international networking of researchers and laboratories, including sharing and dissemination of research information among countries.

- Where possible, Member States of the South-East Asia Region need to establish and ensure inclusion of an appropriate viral hepatitis research agenda (for relevant institutions) into national health policies and

programmes, as well as ensuring adequate funds are allocated for research on viral hepatitis. They should aim to establish a national database of all ongoing research relevant to the viral hepatitis programme, including drug trials and development of vaccine and diagnostic tools, and share this information both within the country and with other countries in the Region.

- Member States should set up a network of institutes engaged in research, such as national centres of excellence, academic institutions and WHO collaborating centres, to support research relevant to national programmes, facilitate close collaboration between researchers and programme managers and promote actionable research.
- They should build/enhance institutional and individual capacity-building for preparing quality research proposals and conducting research that can be applied to prevention and control of viral hepatitis. They should also promote research that determines the influence of environmental, ecological and social factors on the epidemiology of viral hepatitis.

At this stage, four major research areas (strategies) for viral hepatitis have been identified. The examples of research are presented in Table 7.

### **Actions to be initiated during 2013–2014**

- Determine regional and national research priorities for public health, and clinical policies and interventions
- Advocate for, provide technical justification and identify needs to financial institutions and donor agencies, to obtain resources for research in the field of viral hepatitis
- Propose inclusion of an appropriate viral hepatitis research agenda into national health policies and programmes
- Prepare a national database of all ongoing research relevant to the viral hepatitis programme, including drug trials and development of vaccine and diagnostic tools

Table 7: Strategic framework for research (example of research areas)

Strategies	Hepatitis A	Hepatitis B	Hepatitis C	Hepatitis E
1. Monitor the changing epidemiological and virological patterns	For example, monitoring the epidemiological shift of hepatitis A using sero-epidemiological studies  Study the variability of hepatitis A incidence within urban–rural and socioeconomic differences	Determine the prevalence of hepatitis B vaccine escape mutants	Research on effective implementation of hepatitis C risk reduction	Standardize diagnostic reagents for hepatitis E
2. Reduce the risk of transmission	Study the variability and stratification of hepatitis A incidence within urban–rural and socioeconomic differences	Research on effective implementation of hepatitis B risk reduction	Determine the prevalence of hepatitis C in the general population	Determine the morbidity and mortality associated with hepatitis E
3. Assess the impact of intervention	Formulate a hepatitis A prevention strategy based on disease burden and epidemiological shift		Comparative studies of current practices on care and treatment of patients with acute and chronic hepatitis C infection	Determine the effectiveness of introduction of hepatitis E vaccination – needs, programmatic feasibility, cost effectiveness and social acceptance
4. Assess/develop new tools for prevention, diagnosis, care and treatment	Study of introduction of hepatitis A vaccination – needs, programmatic feasibility, cost effectiveness and social acceptance	Comparative studies of the efficacy of current practices for care and treatment of patients with acute and chronic hepatitis B infection	Studies for development of guidelines on standard care and treatment for acute and chronic hepatitis B infection	Operational research on fulminant hepatitis in pregnant women

### **Actions to be initiated during 2014–2015**

- Network of research institutions working in the field of viral hepatitis to be established
- Research proposals on viral hepatitis to be developed and submitted to funding agencies

### **Actions to be initiated during 2015**

- Review the implementation of the strategic framework for research

## **Reference**

- (1) The Global Fund, USAID WHO, UNAIDS, World Bank. Framework for operations and implementation research in health and disease control programs. Geneva: The Global Fund to Fight Aids, Tuberculosis and malaria; 2008 ([http://whqlibdoc.who.int/publications/2008/9292241109\\_eng.pdf](http://whqlibdoc.who.int/publications/2008/9292241109_eng.pdf), accessed 16 October 2013).

## 7. Strategic framework for prevention and control

	Hepatitis A	Hepatitis B	Hepatitis C	Hepatitis E
<b>Goal</b>	<b>Prevent the acquisition and transmission of viral hepatitis</b>			
<b>Strategies</b>	<p>Emphasize the importance of sanitary conditions and personal hygiene</p> <p>Promote the use of effective risk reduction interventions and strategies</p> <p>Determine the need for inclusion of hepatitis A vaccine in routine childhood immunization</p> <p>Formulate a hepatitis A vaccination policy for persons with chronic liver disease</p>	<p>Integrate hepatitis B counselling, screening and referral services into existing service</p> <p>Improve access to hepatitis B screening and referral for diagnoses</p> <p>Maintain adequate infection control practices in health-care and other settings</p> <p>Support implementation of mandatory screening of all blood and blood products</p> <p>Support efforts to prevent iatrogenic transmission of hepatitis B</p>	<p>Integrate hepatitis C counselling, screening and referral services into existing service</p> <p>Improve access to hepatitis C screening and referral for diagnoses</p> <p>Maintain adequate infection control practices in health-care and other settings</p> <p>Support implementation of mandatory screening of all blood and blood products</p> <p>Support efforts to prevent iatrogenic transmission of hepatitis C</p>	<p>Emphasize the importance of sanitary conditions and personal hygiene among persons at greater risk (pregnant woman)</p> <p>Promote the use of effective risk reduction interventions and strategies</p>



	Hepatitis A	Hepatitis B	Hepatitis C	Hepatitis E
		<p>Implement harm reduction interventions among injecting drug users</p> <p>Implement safe practice guidelines for tattooing, piercing procedures and acupuncture</p> <p>Deliver a dose of hepatitis B vaccine at birth as part of an integrated package of maternal and neonatal care, if not yet implemented</p> <p>Extend hepatitis B vaccination to all health professionals and other people considered to be in high-risk groups</p>	<p>Implement harm reduction interventions among injecting drug users</p> <p>Implement safe practice guidelines for tattooing, piercing procedures and acupuncture</p>	

## 7.1 Prevention of hepatitis A and E virus infection

**Strategy – emphasize the importance of sanitary conditions and personal hygiene and promote the use of effective risk reduction interventions and strategies**

The most important approaches to preventing both sporadic cases and outbreaks of HAV and HEV infection are improvement of sanitation, adequate supplies of safe drinking water and a proper sewage system, combined with personal hygiene practices such as regular handwashing. The only way to break the continued transmission of HAV and HEV is to improve people's hygienic behaviour and to provide them with certain basic needs of drinking water and proper cooking, washing and bathing facilities and sanitation. WHO should continue to advocate the provision of safe water and proper sanitation, support countries' efforts to improve hygienic practices and provide technical

assistance for preparedness, detection and response to outbreaks of HAV and HEV. The Member States should provide and monitor safe water for drinking and household use, improve sanitation, and foster behaviour change for improving hygienic practices.

### **Actions to be initiated during 2013–2014**

- Provision of safe water and proper sanitation to be advocated at national and regional levels and the roles and responsibilities of the health sector, water and sanitation and community to be clearly defined
- Develop workplan to foster behaviour change for improved hygienic practices

### **Actions to be initiated during 2014**

- Strengthen preparedness, detection and response to outbreaks of viral hepatitis.

## **7.2 Hepatitis A and E immunization**

### **Strategy – determine the need for inclusion of hepatitis A vaccine in routine childhood immunization and formulate a hepatitis A vaccination policy for persons with chronic liver disease**

Several hepatitis A vaccines are available internationally. All are similar in terms of how well they protect people from the virus and their side-effects. No vaccine is licensed for children younger than one year of age.

Nearly 100% of people will develop protective levels of antibodies to the virus within 1 month after a single dose of the vaccine. Even after virus exposure, one dose of the vaccine within 2 weeks of contact with the virus has protective effects. Millions of people have been immunized with no serious adverse events. The vaccine can be given as part of regular childhood immunizations programmes and with vaccines commonly given for travel.

Planning for large-scale immunization programmes should involve careful economic evaluations and consider alternative or additional prevention methods, such as better sanitation and health education for improved hygiene.

Whether or not to include the vaccine in routine childhood immunizations depends on the local context, including the level of risk for children and seroprevalence in adults. Several high-income countries have introduced the vaccine in routine childhood immunizations. Other countries, generally of low endemicity, recommend the vaccine for persons at increased risk of hepatitis A, including travellers to countries where the virus is endemic, men who have sex with men, or persons with chronic liver disease (because of their increased risk of serious complications if they acquire HAV infection). Recommendations for hepatitis A vaccination in outbreaks should also be site specific, including the feasibility of rapidly implementing a widespread immunization campaign. Vaccination to control community-wide outbreaks is most successful in small communities, when the campaign is started early and when high coverage of multiple most at-risk age groups is achieved. Vaccination efforts should be supplemented by health education to improve sanitation and hygiene practices.

## **Hepatitis E vaccine**

At present, no commercially available vaccines exist for the prevention of hepatitis E. However, several studies for the development of an effective vaccine against hepatitis E are in progress and recently only China had patented this vaccine for internal use. Further studies are required to determine the need for hepatitis E vaccination in countries with high incidence of this infection.

### **Actions to be initiated during 2013–2014**

- Studies to determine the need for inclusion of hepatitis A vaccine in routine childhood immunization and for persons with chronic liver diseases

### **Actions to be initiated during 2014**

- Formulate a hepatitis A vaccination policy for persons with chronic liver disease

### **Actions to be initiated during 2015**

- Studies to determine the need for introduction of hepatitis E vaccine in countries with high incidence of HEV infection.

## 7.3 Prevention of hepatitis B and C virus infection

### Strategy – promote the use of effective risk reduction interventions and strategies:

- Integrate hepatitis B and hepatitis C counselling, screening and referral services into existing service
- Improve access to hepatitis B and hepatitis C screening and referral for diagnoses
- Maintain adequate infection control practices in health-care and other settings
- Support implementation of mandatory screening of all blood and blood products
- Support efforts to prevent iatrogenic transmission of hepatitis B and hepatitis C
- Implement harm reduction interventions among injecting drug users
- Implement safe practice guidelines for tattooing, piercing procedures and acupuncture

Communities need to be aware that hepatitis B and C viruses are transmitted between people by contact with the blood or other body fluids (i.e. semen and vaginal fluid) of an infected person. Modes of transmission are the same for HIV, but HBV is many times more infectious. HBV can survive outside the body for at least 7 days. During that time, the virus can still cause infection if it enters the body of a person who is not infected. The virus incubation period is 90 days on average, but can vary from about 30 to 180 days. HBV may be detected 30 to 60 days after infection and persist for widely variable periods of time. Hepatitis B prevention activities should aim to reduce common modes of transmission (see Table 8).

Persons found to be infected with HCV should:

- be referred for education and counselling on safe behaviour, together with consideration of partner notification;
- be assessed with respect to options for care and treatment, including consideration of immunization with hepatitis A and B vaccine (to protect their liver);

Table 8: Common modes of transmission of hepatitis B and C virus

Mode of transmission	HBV	HCV
Perinatal (from mother to baby at birth)	High	Unknown
Early childhood infections (through contact with infected individuals)	High	Unknown
Transfusions of unscreened blood/blood products	High	High
Unprotected sexual intercourse	High	Low
Sharing equipment for internal drug use	High	High
Piercing, tattooing, acupuncture and shaving with contaminated instruments	High	High

- receive early and appropriate medical management, including antiviral therapy if appropriate;
- get regular monitoring for early diagnosis of liver disease.

Safe injections, safe invasive medical and surgical practices (standard precautions) and blood safety are the most important components of prevention of hepatitis B and C infection in low- and middle-income countries, where these infections are associated with medical treatment or interventions. Top priority should be given to implementing and monitoring safe injections and blood safety at all health-care facilities.

### Actions to be initiated during 2013–2014

- Review current national policies on integration of hepatitis B and hepatitis C counselling, screening and referral services into existing service
- Review current national policies on mandatory screening of blood and blood products for hepatitis B and hepatitis C, considering the use of new highly specific and sensitive standardized diagnostic kits

### Actions to be initiated during 2014–2015

- Improve access to hepatitis B and hepatitis C screening and referral for diagnoses
- Monitor and effectively implement safe injection practices in all health-care facilities, through advocacy, education and monitoring of standard precautions

- Implement harm reduction interventions among injecting drug users
- Implement safe practice guidelines for tattooing, piercing procedures and acupuncture
- Support efforts to prevent iatrogenic transmission of hepatitis B and hepatitis C

### **Actions to be initiated during 2015**

- Review the implementation of the strategic framework for prevention

## **7.4 Hepatitis B immunization**

**Strategy – deliver a dose of hepatitis B vaccine at birth as part of an integrated package of maternal and neonatal care, if not yet implemented and extend hepatitis B vaccination to all health professionals and other people considered to be in high-risk groups**

All infants should receive the hepatitis B vaccine: this is the mainstay of hepatitis B prevention. The vaccine can be given as either three or four separate doses, as part of existing routine immunization schedules. In areas where mother-to-infant spread of HBV is common, in high- and intermediate-prevalence countries, the first dose of monovalent vaccine should be given as soon as possible after birth (i.e. within 24 hours).

The complete vaccine series induces protective antibody levels in more than 95% of infants, children and young adults (if they have not been infected before, i.e. if the mother is infected and transmits the virus before the child is vaccinated, and no immunoglobulins are given simultaneously within 24 hours of birth, vaccination can fail to protect the child). After the age of 40 years, protection following the primary vaccination series drops below 90%. At 60 years of age, protective antibody levels are achieved in only 65% to 75% of those vaccinated. Protection lasts at least 30 years and should be lifelong.

Countries should examine their epidemiological situation (age-specific prevalence of anti-HBc), and immunization history (number of years of infant vaccination programme and vaccination coverage of infants), and take into consideration the programmatic and financial consequences, in order to decide whether to offer vaccination to all adolescents who have not been previously vaccinated, before the age

of 18 years. Indeed infection generally occurs either in early childhood or in adulthood after initiation of sexual activity and/or other at-risk activities.

Vaccination of people in high-risk groups should be considered, after examination of the epidemiological situation and programmatic issues (appropriate settings to reach the persons at risk, such as occupational health services in health institutions, sexually transmitted infection (STI) clinics, services for harm reduction in substance abusers), including:

- those at occupational risk of HBV infection, primarily health-care workers;
- persons with high-risk sexual behaviour;
- partners and household contacts of HBV-infected persons;
- injecting drug users;
- persons who frequently require blood or blood products;
- persons undergoing renal dialysis;
- recipients of solid organ transplantation.

The vaccine has an outstanding record of safety and effectiveness. Since 1982, over one billion doses of hepatitis B vaccine have been used worldwide. In many countries where 8% to 15% of children used to become chronically infected with HBV, vaccination in early infancy has reduced the rate of chronic infection to less than 1% among immunized children.

### **Actions to be initiated during 2013–2014**

- Design a programme for delivery of the dose of hepatitis B vaccine at birth, as part of an integrated package of maternal and neonatal care, if not yet implemented
- Commence piloting a programme for delivery of the dose of hepatitis B vaccine at birth in selected districts, if not yet implemented

### **Actions to be initiated during 2014–2015**

- Review the pilot programme and, based on the results, modify the national strategy for hepatitis B immunization
- Study the appropriateness and feasibility of a national policy to extend hepatitis B vaccination in “catch-up programmes” and to all health professionals and other people considered to be in high-risk groups

## 8. Strategic framework for education

	Hepatitis A , B, C and E
Goal	Build knowledge and awareness regarding viral hepatitis prevention, vaccination, risk factors, treatment and medical management
Strategies	<p>Increase the knowledge of viral hepatitis among the general population and promote a healthy lifestyle among persons who are newly diagnosed or living with chronic viral hepatitis</p> <p>Improve and expand the knowledge of viral hepatitis among health- and human-service providers</p>

Studies conducted in Bangladesh, India, Indonesia and Nepal have revealed very low knowledge and awareness about all forms of viral hepatitis, including the route of transmission and risk factors (1–10). A high proportion of the population is not aware that the infected person may remain asymptomatic and undiagnosed for long periods, and that the diseased person may develop chronic complications like liver failure and liver cancer. The situation is similar in other countries of the Region. As a result of technical progress in the last 5 years, information on prevention and control of viral hepatitis is available through the Internet. However, this does not influence the general population, owing to limited access and the low literacy rate. Bangladesh, Bhutan, Nepal, India and Timor-Leste have adult literacy rates in the range of about 40–60%, while all other countries of the WHO South-East Asia Region have literacy rates above 90% (11, 12).

The national authorities of all countries of the Region realize the importance of health education and health promotion. However, owing to limited resource allocation, a viral hepatitis awareness programme has not yet been implemented.



## 8.1 Education programmes for general and at-risk populations

### **Strategy – increase the knowledge of viral hepatitis among the general population and promote a healthy lifestyle among persons who are newly diagnosed or living with chronic viral hepatitis**

An educational strategy to increase the knowledge of viral hepatitis among the general population and promote a healthy lifestyle among persons who are newly diagnosed or living with chronic viral hepatitis includes targeted outreach to populations at risk. It can raise awareness of viral hepatitis as a health concern, increase knowledge regarding the benefits of prevention and care, and encourage populations to seek and accept preventive and protective interventions such as vaccination, testing, care and treatment. Accessing medical care will also provide opportunities to educate at-risk groups about preventive and protective measures.

The health education and awareness programmes should incorporate interventions that meet the following goals:

- achieve better understanding of infection, transmission, prevention, care and treatment of viral hepatitis in at-risk and general populations;
- achieve reduction of outbreaks of HAV and HEV by improving sanitary behaviour and consumption of safe water;
- achieve the highest (more than 95%) hepatitis B vaccination rates among children and increase vaccination of at-risk adults;
- educate pregnant women and women of childbearing age about prevention of hepatitis B;
- achieve reduction of perinatal HBV infection and improvement of infant immunization rates;
- achieve increased testing rates in at-risk populations;
- reduce stigmatization of chronically infected people;
- promote safe injections;
- provide culturally and linguistically appropriate educational information for all persons who have tested positive for chronic HBV or HCV infection and those who are receiving treatment;

- encourage notification of household contacts of infected people to be tested for HBV and HCV and encourage hepatitis B vaccination of close contacts;
- support the establishment of collaboration with patient and advocacy groups for viral hepatitis and other partners involved in the viral hepatitis prevention and control programme.

## Ways to communicate

### Media

There is a need for broader community education, which should include print, multimedia (TV and radio), social media and educational materials about viral hepatitis for the public, as well as interpersonal means of communication.

### School curricula

The lack of knowledge and awareness about viral hepatitis in the general population suggests that integration of viral hepatitis and liver-health education into the existing health-education curricula in schools will help to eliminate the stigma of those chronically infected and improve the prevention of viral hepatitis. Schools in many countries already have health education on HIV and it is possible to add education about viral hepatitis to this programme.

### Community leaders

Community and religious leaders should also be actively involved in the viral hepatitis education campaign.

### Partnerships with health-care providers and nongovernmental organizations

The ministries of health, with technical assistance from WHO, should work with other ministries and local governments to form partnerships with health-care providers, NGOs, schools and appropriate community representatives, to develop awareness programmes and campaigns to educate the general public and at-risk populations about viral hepatitis. These programmes should share resources that are linguistically and culturally appropriate and support integration of education on viral hepatitis and liver health into other health programmes. Successful field-tested programmes should

serve as models for interventions, and existing material should be used as a basis for producing linguistically and culturally relevant materials.

### **Innovations for reaching the less literate**

Innovative approaches should be developed to address populations that have low education and limited access to health-education programmes. An evaluation of health-education programmes is required to ensure that they are effectively targeting the general public and at-risk people and populations. The results of this evaluation will help formulate future initiatives.

### **Patients' and advocacy groups**

Patients' and advocacy groups for viral hepatitis became active in the USA and many European countries, supporting their governments' efforts to implement prevention and control of viral hepatitis (13). These groups range from small groups of volunteers and a few paid professionals to full membership organizations with assemblies, boards, directors, advisers and trustees. The strengths of patients' and advocacy groups are their ability to get messages across, information dissemination in various means (web sites, newsletters), and an ability to network more easily than bureaucracies and other groups. The message and language can be adapted to target patient groups. Multilingualism – working in many languages – is beneficial, especially in reaching individuals in some hard-to-reach groups.

Cultural sensitivity and broad support from professional bodies/associations and parliamentarians, media support, trust and respect of the public, positive image and common purpose play an important role in advocacy of the viral hepatitis prevention and control programme. Intensive lobbying by patients and advocacy groups helps in the generation of resources that are urgently needed for implementation of the viral hepatitis programme.

### **World Hepatitis Day**

The date 28 July has been designated as World Hepatitis Day, in order to provide an opportunity for education to promote greater understanding and awareness of viral hepatitis as a global health problem. With the technical assistance of the WHO Regional Office for South-East Asia, the Member States successfully marked the first World Hepatitis Day on 28 July 2011, and mass education campaigns were organized in all

countries. This effort should continue and the World Hepatitis Day should be used as a means for promoting the prevention and control of viral hepatitis.

### **Actions to be initiated during 2013–2014**

- Develop and produce materials for a general audience on prevention of viral hepatitis, emphasizing that everyone is affected; most affected people do not know they are “infected” and most do not have any visible symptoms; include patients stories and tie a link to local outreach
- For hepatitis B awareness, develop and distribute messages about mother-to-child transmission and demographic groups with the highest rate of infection
- For hepatitis C awareness, develop and distribute messages about blood transfusion and prior and past drug use
- Start an education campaign for the general public, to reduce unnecessary injections

### **Actions to be initiated during 2014**

- Organize World Hepatitis Day and use it for mass campaigns for education and awareness in all the Member States of the Region
- Develop and disseminate information for promotion of a healthy lifestyle among persons who are newly diagnosed or living with hepatitis B or C

## **8.2 Education programmes for health-care providers**

### **Strategy – improve and expand the knowledge of viral hepatitis among health- and human-service providers**

The studies carried out in the countries of the WHO South-East Asia Region reveal inadequate knowledge about the risk factors for different forms of viral hepatitis as well as the short-term and long-term consequences of acute and chronic HBV and HCV infection among primary health-care providers and family doctors, including nurses and midwives. It was learnt that the majority had some knowledge regarding the mode of transmission and attitude towards patients with HBV infection. However, there are misconceptions about prophylaxis, vaccination, treatment and case-management of chronic HBV infection. In addition, it has been found that the knowledge of resident

doctors, nurses and technicians is not adequate regarding various aspects of post-exposure prophylaxis (PEP) related to HBV infection (like the immediate steps to be taken after an exposure), the PEP regimens, and whom to contact in the institution for obtaining PEP; it has also been shown that HBV vaccination is not adequate (10, 14, 15). Similarly, general health practitioners have been found to have limited knowledge regarding HCV infection (16–19). Only limited numbers of clinicians are familiar with management of severe HAV and HEV infection (20).

Based on these findings, the following needs to be achieved on a priority basis:

- improving the knowledge of health-care providers about viral hepatitis testing, care and treatment; this is the key to maximizing the benefits afforded by new viral hepatitis testing and treatment options;
- clarity among primary health-care providers, who should know about whom to test for viral hepatitis, how to interpret test results, what information is needed by their patients, and when patients need recommended preventive and care services;
- increased skills among health personnel caring for persons living with viral hepatitis; they should be taught how to manage cofactors that hasten the progression of liver disease (e.g. alcohol use) in monitoring patients for signs of disease progression and in referring patients for consultation and therapy, when appropriate;
- guidance for clinicians who treat patients with viral hepatitis, regarding the use of more effective but more complex regimens, including decision support tools (e.g. standing orders and telemedicine consultations);
- as testing options increase and therapeutic options become more effective and better tolerated, the need for a well-informed health-care workforce will become paramount;
- to be effective, education of health-care providers should be initiated as early as possible, including as part of medical and other health professional school curricula, and this should continue throughout their careers;
- training centres can serve as important resources for improving provider knowledge regarding viral hepatitis, along with professional medical societies that provide health-care professionals with continuing education.

## Ways to educate health-care providers

It is important to note that educational programmes and materials for health-care providers should focus on improving provider awareness and adherence to practised guidelines for viral hepatitis. The educational programmes should be targeted to include all health-care providers, including the staff of drug-treatment facilities and practising acupuncturists and tattoo and traditional medicine practitioners.

Educational institutions like medical schools, universities and public health institutions should develop improved curricula to ensure that the graduates are knowledgeable about viral hepatitis. The curricula should include information on disease prevalence, risk factors, preventive action, appropriate testing and diagnosis, selection of patients for timely testing, treatment of acute and chronic hepatitis and appropriate follow-up and monitoring of chronically infected hepatitis B and hepatitis C patients and those who are susceptible to infection.

Leading institutions in the field of viral hepatitis should conduct courses for continuing medical education and activities related to viral hepatitis. These courses should be offered to doctors and nurses working in various medical care facilities. Questions regarding prevention, testing, care and management of viral hepatitis should be included in certification or re-certification examinations. The following topics could be suggested for lectures/seminars and workshops:

- infection control guidelines;
- viral hepatitis prevention interventions for the clinical setting;
- viral hepatitis screening and vaccination;
- managing acute hepatitis;
- severe HAV infection;
- severe HEV infection in pregnant woman;
- managing chronic HBV and HCV;
- managing HBV/HCV, HBV/HIV, HCV/HIV and HBV/HCV/HIV coinfection;
- monitoring for and managing fibrosis and liver cancer;
- teaching patients liver self-care;
- treating injecting drug users for HCV;
- when to consult with or refer to a specialist;
- managing patients through liver transplantation.

Educational programmes on viral hepatitis should include targeted outreach and enrolment of providers who work in high-risk settings, for example STI and HIV clinics.

A new approach is required to improve the knowledge of medical personnel working in hospitals and other health-care facilities who are at risk of exposure to infected blood and body fluids, and who are therefore vulnerable to HBV and HCV infection. In addition, staff of drug-treatment and needle-exchange programmes and medical staff of correctional facilities like prisons should participate in viral hepatitis educational programmes. Providing standardized education to staff of drug-treatment and needle-exchange programmes and correctional facilities will ensure that at-risk and HBV- and HCV-infected persons in these settings receive consistent and accurate information.

It should be obligatory for the health administration to offer hepatitis B vaccination to all health-care workers who may be exposed to blood, blood products and patient fluid. Successful interventions known to prevent exposure to/transmission of bloodborne infection include training on general safety, training specific to the prevention of needle-stick injuries, standardization of practice, staffing and workload adjustments, and use of protective devices.

Special training for doctors is required to enable them to successfully organize care and management of a large number of patients during HAV and HEV outbreaks, which mainly occur during or after the rainy season. Clinicians also have limited knowledge and understanding about the management of HEV infection in pregnant women.

The number of HAV and HEV cases and outbreaks can be prevented by improving sanitation and the quality of water. There is a need to provide intensive training to water and sanitation staff on how to prevent and contain HAV and HEV outbreaks.

To improve knowledge and awareness of viral hepatitis among health-care providers, the education programmes should include the following components:

- information about the prevalence and incidence of acute hepatitis A, and hepatitis E and acute and chronic hepatitis B and hepatitis C infection in the general population and in at-risk populations (injecting drug users, sex workers, prisoners);
- standardized information about transmission, risk factors and prevention of hepatitis A, B, C and E and hepatitis A and B immunization;
- the importance of screening for viral hepatitis markers;

- guidance on screening for risk factors associated with hepatitis B and C;
- information about methods of testing and interpretation of results;
- when to refer the patient to a specialist;
- information about medical management of acute viral hepatitis;
- medical management of chronically infected hepatitis B and hepatitis C patients;
- how to select patients for antiviral therapy;
- information about prevention of HBV and HCV transmission in hospital and other health-care settings.

### **Actions to be initiated during 2013–2014**

- Compile existing viral hepatitis training resources for public health and community health providers
- Develop health-provider toolkits summarizing key information regarding the availability of diagnostic, vaccination, care and treatment services for viral hepatitis
- Facilitate collaborative work of universities and medical associations, to promote awareness of viral hepatitis at their conferences and meetings and in newsletters and guidance documents

### **Actions to be initiated during 2014–2015**

- Identify and foster “champions” among institutions, clinicians and health-care workers, who will train their peers on implementing standards of care and management for viral hepatitis
- Expand monitoring of primary care providers by clinicians who are experienced in management of chronic viral hepatitis, and expand consultation network support
- Educate practitioners in health-care settings, tattoo studios and other settings where there may be a risk of HBV or HCV transmission.

### **Actions to be initiated during 2015**

- Review the implementation of the strategic framework for education



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# 9. Strategic framework for medical care and treatment

	Hepatitis A ,B C, and E
Goal	Develop and maintain services to provide the highest quality of viral hepatitis care and treatment
Strategies	<div>Develop standard procedures for management of acute viral hepatitis and guidance on counselling, support and care for infected individuals</div> <div>Assure timely access to chronic HBV and HCV diagnosis, care, treatment and supportive services and their integration into primary care settings</div> <div>Establish programmes to support care and treatment for marginalized individuals and populations</div> <div>Developm guidelines for the clinical management, counselling and care of people with viral hepatitis, including updating such documents when new WHO guidance becomes available</div>

In the last 10 years, significant progress has been made in the development of new drugs and medicines for treatment of chronic hepatitis B and C infections. At this stage, the treatment options are still limited, owing to high cost and limited access to these medicines. In the current situation, it is important to analyse existing care and treatment practices for the medical care and treatment of viral hepatitis in the Member States and to develop suitable strategies for its improvement.

## 9.1 Management of acute viral hepatitis

### Strategy – develop standard procedures for management of acute viral hepatitis and guidance on counselling, support and care for infected individuals

The single most important issue in the management of acute viral hepatitis is that, in the great majority of cases, treatment should be supportive and does not require medication.

Whereas most acute infections are asymptomatic, when symptoms are present they appear to be similar for all viral hepatitis. It is important to establish which virus is involved, as the risks of progression differ:

- *hepatitis A*: self-limiting – the rate of fulminant hepatic failure (FHF) rate is less than 1%;
- *hepatitis B*: self-limiting in 95% of cases (adults only), but not in children under the age of 5 years;
- *hepatitis C*: self-limiting in 20–50% of cases;
- *hepatitis E*: self-limiting – the overall mortality rate in FHF is 1–3%; in pregnant women the rate is 15–25%.

A second important issue is the identification of risk groups. In pregnant women, for example, it is very important to exclude HEV. In all cases, risk groups for severe hepatitis should be identified; usually, this affects older adults and those with underlying chronic liver disease. Acute fulminant hepatitis may occur at any age.

For the management of acute hepatitis, the following need to be considered:

- a case of acute “hepatitis” maybe caused by a virus or a toxin, or may be the first manifestation of a chronic liver disease;
- acute viral hepatitis is almost always self-limiting;
- in almost every case, it is best to do nothing (except to stop medications such as the oral contraceptive pill);
- there is no role for vitamins; in low- and middle-income countries in particular, intravenous vitamins are often given unnecessarily;
- there is no role for restriction of proteins in uncomplicated acute hepatitis; in low- and middle-income countries, patients may already be deprived of proteins; this leads to protein deficiency, with the associated complications;

- exercise should be started as soon as the patient feels fit to do so; there is no need to keep patients in bed;
- a raised serum alanine aminotransferase (ALT) level is the best indicator of acute hepatic injury, but does not reflect the severity of the disease; values for bilirubin and international normalized ratios are required for this;
- all forms of acute viral hepatitis show the same symptoms;
- the endemicity of the conditions should be taken into account – e.g. hepatitis A predominantly affects children in endemic areas;
- it should be ascertained whether the condition is an acute infection or a flare-up of a silent chronic infection;
- other chronic liver diseases may present acutely – for example, autoimmune hepatitis;
- consideration should be given to the transmission, and thus prevention and vaccination where appropriate;
- in a pregnant woman with HBV infection, the infant should be protected with hepatitis B vaccine.

### Management of acute HAV infection

The subjective impression of the patient should guide the doctor's approach. Neither hospital admission, quarantine or bed rest is necessary. The treatment should be conservative and supportive. There is no specific medication for HAV infection. Hygiene is very important – hands should always be washed after bathroom use. The management should focus on treating the symptoms and identifying the small proportion of patients with a particular risk of developing FHF. Oral contraceptive use and hormone replacement therapy should be stopped to avoid cholestasis. Alcohol consumption is not advised. HAV has only acute clinical manifestation.

### Management of acute HBV infection

Spontaneous recovery after acute infection with HBV occurs in 95–99% of previously healthy adults.

Antiviral therapy is not therefore likely to improve the rate of recovery and is not required unless the disease is accompanied by a non-hepatic complication such as polyarteritis nodosa. In such cases, and in immunocompromised individuals (e.g. those with chronic renal failure), antiviral therapy with lamivudine may be recommended. In fulminant hepatitis, meticulous intensive care may improve the survival.

Full recovery with development of anti-HBsAg provides long-term protection.

## Management of acute HCV infection

In acute HCV infection, serum HCV RNA is usually detected before the appearance of anti-HCV antibodies and this is often the only diagnostic indicator of the conditions. Acute HCV infection often becomes chronic, especially in asymptomatic individuals. However, the infection spontaneously resolves in up to 50% of patients who present the symptoms (1). Spontaneous resolution is less likely after 12 weeks of infection. Treatment of hepatitis C in the acute stage has resulted in better sustained virological response (SVR). Studies using conventional interferon and peginterferon alfa for 24 weeks, have achieved high rates of SVR in acute hepatitis C (2–6). The objective of antiviral treatment in acute hepatitis C is to prevent the development of HCC. Patients should be advised to totally stop consumption of alcohol.

## Management of acute HEV infection

Treatment is supportive only. Pregnant women are a special risk category. Pregnant women with acute hepatitis E infection have an approximately 15% risk of FHF. The mortality rate is high, ranging from 5% to 25% in different studies. HEV infection causes mortality in up to 25% of pregnant women in the third trimester of pregnancy. The management should focus on treating the symptoms.

## Actions to be initiated during 2013–2014

- Establish one or more national referral centres for the care and treatment of viral hepatitis, for coordination of medical care and treatment of viral hepatitis in the country, and to organize seminars, meetings and training in the field of care and treatment
- Review common practices and procedures for the management of acute viral hepatitis

### **Actions to be initiated during 2014–2015**

- Establish a network among the national referral centres of Member States for medical care and treatment of viral hepatitis
- Develop standard procedures for the management of acute viral hepatitis and guidance on counselling, support and care for infected individuals

## **9.2 Medical care and treatment of chronic HBV and HCV infections**

### **Strategies:**

- **Assure timely access to chronic HBV and HCV diagnosis, care, treatment and supportive services and their integration into primary care settings**
- **Establish programmes to support care and treatment for marginalized individuals and populations**
- **Develop guidelines for the clinical management, counselling and care of people with viral hepatitis, including updating such documents when new WHO guidance becomes available**

People who are infected with HBV or HCV may develop a chronic infection that can lead to cirrhosis. The damage that results increases the risk of liver cancer. This risk may be as high as 200 times greater for people who have chronic HBV or HCV infection than for the general population.

### **Chronic HBV**

The major goals of anti-HBV therapy are to prevent the development of progressive liver disease, specifically cirrhosis and liver failure, and prevent the development of HCC and subsequent death. To date, no conclusive evidence from randomized controlled trials of anti-HBV therapy has demonstrated a beneficial impact on any of these primary clinical outcomes because cirrhosis, HCC and death often do not occur for many years after infection with HBV and therefore long-term evaluation of therapy would be required to demonstrate benefit. As a consequence, most published reports of anti-HBV therapy use changes in short-term virologic, biochemical, and histologic parameters to infer the likelihood of long-term benefit. It is important to understand the limitations of this practice when assessing potential benefit.

Currently, in industrial countries, at least seven medicines are approved for treating chronic HBV infection in adults. These agents, categorized as either interferons (interferon-alfa-2b and peginterferon-alfa-2a) or nucleoside or nucleotide analogues (lamivudine, adefovir, entecavir, tenofovir and telbivudine), may be used as monotherapy or in combination. Interferon use has a defined, self-limited course; in contrast, therapy with nucleoside or nucleotide analogues can be long-term, often indefinite, treatment.

Several professional organizations, including the American Association for Study of Liver Diseases (AASLD), the Asia Pacific Association for the Study of the Liver (APASL) and the European Association for the Study of Liver (EASL) have developed guidelines for treating chronic HBV infection (7–9).

An informal WHO consultation of experts concluded that: chronic HBV is a major public health problem in emerging nations; all HIV-infected persons should be screened for HBV infection; HIV/HBV coinfecting persons should be treated with therapies that are active against both viruses and that reduce the risk of resistance; and standards for the management of chronic HBV infection should be adapted to resource-constrained settings (10). The findings and recommendations of this consultation do not constitute formal WHO policy.

## Chronic HCV

Similarly to anti-HBV therapy, the goal of therapy is to eradicate HCV infection in order to prevent the complications of HCV-related liver disease, including necro-inflammation, fibrosis, cirrhosis, HCC and death. The end-point of therapy is SVR; intermediate end-points are used during the standard of care treatment to assess the likelihood of an SVR and tailor treatment duration. They include measurements of HCV RNA levels at 4, 12 and 24 weeks of therapy, which are interpreted in comparison to the baseline HCV RNA level. When HCV is eradicated, necro-inflammation ceases and fibrosis progression is halted in non-cirrhotic patients.

The standard of care therapy for patients with chronic HCV infection has been the use of both peginterferon-alfa-2a and ribavirin. These drugs are administered for either 48 weeks (HCV genotypes 1, 4, 5 and 6) or 24 weeks (HCV genotypes 2 and 3), inducing SVR rates of 40–50% in those with genotype 1 and 80% or more in those with genotypes 2 and 3 infections (11, 12). Once achieved, an SVR is associated with long-term clearance of HCV infection, which is regarded as a virologic “cure”, as well as with improved morbidity and mortality.



In the last 2–3 years, direct-acting antiviral agents (DAAs) (13–16) have been developed and several single-nucleotide polymorphisms associated with spontaneous and treatment-induced clearance of HCV infection have been identified (17, 18).

Although both peginterferon-alfa-2a and ribavirin are vital components of therapy, the emergence of DAAs has led to a substantial improvement in SVR rates and the option of abbreviated therapy in many patients with genotype 1 chronic HCV infection.

Recently, AASLD, APASL and EASL have developed new clinical guidelines for the treatment of chronic HCV infection (19–21).

In February 2012, WHO headquarters organized a consensus meeting on “Guidance on prevention strategies for viral hepatitis B and C in people who inject drugs; surveillance and antiviral management in people with HIV and viral hepatitis B and C coinfections” (22).

The WHO Global Hepatitis Programme has initiated development of the HCV guidelines. It is expected to consolidate treatment guidelines for the management of chronic hepatitis B and C and coinfections with HIV and will be released in 2013.

### **Actions to be initiated during 2013–2014**

- Review accessibility for diagnosis, care and treatment of chronic viral hepatitis

### **Actions to be initiated during 2014–2015**

- Develop national and regional plans of action to strengthen capacity for medical care and treatment of chronic viral hepatitis
- Evaluate current protocols used for treatment of chronic hepatitis B and C patients

### **Actions to be initiated during 2015**


- Member States to participate in field-testing and implementation of the treatment protocols for management of chronic hepatitis B and C (including HIV coinfections).

- Conduct operational research for improved care and treatment of chronic HBV and HCV infection
- Involve professional organizations in development of guidelines and supporting the development of policies for the prevention, care and treatment of viral hepatitis

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## 10. Summary of operational work required for implementation of the *Regional strategy for prevention and control of viral hepatitis* by the Member States and WHO

### 10.1 Strategic framework for policy, planning, advocacy and resource mobilization

#### Policy and planning

##### WHO

- Nominate a focal point in the Regional Office responsible for the coordination of work for prevention and control of viral hepatitis
- Establish a viral hepatitis working group in the Regional Office
- WHO country representatives to identify a focal point who will be responsible for supporting viral hepatitis programmes at country level
- Establish a regional technical advisory group for viral hepatitis

## Member States

- Identify person or establish the unit responsible for the coordination of prevention and control of viral hepatitis at the ministry of health
- Establish a national committee on viral hepatitis; this committee should be responsible for the development of a national strategy and programmes on prevention and control of viral hepatitis, and its supervision, coordination, implementation and monitoring at the national level

## Communication for advocacy

### WHO

- Advocate prevention and control of viral hepatitis with decision-makers and leaders and connect different organizations and groups for advocacy

## Member States

- Build strong relationships with the media, to expand and improve the quality of coverage of viral hepatitis programmes
- Build strong relationships with decision-makers and leaders to encourage effective action and ensure the interests of people with viral hepatitis are heard and addressed

## Resource mobilization

### WHO

- Develop a strategy for resource mobilization and a list of priorities for funding
- Identify potential proposal writers for funding purposes
- Identify potential financial institutions interested in providing resources for the prevention and control of viral hepatitis
- Advocate fundraising for viral hepatitis in various meetings, symposiums, forums and high-level decision-making gatherings
- Organize meetings and seminars with potential donors, for fundraising purposes

## Member States

- Involve high-level government officials and dignitaries in the process of fund raising
- Build relationships with national/international business communities and organizations to provide a forum for raising donations
- Regularly update community and donor agencies regarding resources that have been received for the viral hepatitis programme and how effectively it has been used

## 10.2 Strategic framework for surveillance

### WHO

- Support countries to establish a national viral hepatitis surveillance system
- Facilitate integration of viral hepatitis surveillance in the other disease surveillance systems
- Support countries to conduct an evaluation of the national viral hepatitis surveillance system; a standard protocol should be developed
- The evaluation should at least include an assessment of the attributes of the existing surveillance system, including completeness, data quality and accuracy, timeliness, sensitivity, specificity, positive predictive value, representativeness and stability. The results of evaluation should be used to formulate detailed technical guidelines and standards for surveillance of viral hepatitis and published in a report
- Support countries in the development of standard protocols for the core surveillance of acute HAV, acute HEV and acute and chronic HBV and HCV infections. There is a need to revise the standardized case definition, case-reporting forms, including case evaluation, and follow-up. In addition, it is crucial to support development and implementation of automated data-collection systems
- Support countries in conducting targeted surveillance, including serological testing and to monitor the incidence and prevalence of viral hepatitis infection in populations that are not fully captured by core surveillance

- Facilitate establishment in Member States of a national referral centre for viral hepatitis surveillance and prevention, as well as a referral centre for laboratory diagnoses of viral hepatitis, to coordinate a network of laboratories
- Support countries' efforts to carry out prequalification of viral hepatitis diagnostics and quality assurance

### Member States

- Conduct situational analysis of the burden of viral hepatitis and establish a national viral hepatitis surveillance system
- Develop standard protocols for the viral hepatitis core and targeted surveillance
- Establish a national referral centre for laboratory diagnosis of viral hepatitis
- Integrate viral hepatitis surveillance in other diseases surveillance systems
- Carry out prequalification diagnostics for viral hepatitis and develop national standardized protocols for testing samples for viral hepatitis
- Ensure national capacity development and implementation of national viral hepatitis programmes
- Allocate and mobilize resources for the viral hepatitis programme

## 10.3 Strategic framework for research

### WHO

- Facilitate the identification of regional and national research priorities for public health, and clinical policies and interventions
- Undertake advocacy, provide technical justification and identify needs to financial institutions and donor agencies for obtaining resources for research in the field of viral hepatitis
- Collaborate with Member States and technical partners in building research capacity based on identified need and clear timelines, at national, institutional and individual levels

- Assist with the design of operational research protocols and coordinate multicentric studies to address the challenges in the viral hepatitis prevention and control programme in an effective manner
- Facilitate national and international networking of researchers and laboratories, including sharing/dissemination of research information among countries by various means, including through the *WHO South-East Asia Journal of Public Health*

### Member States

- Establish and ensure inclusion of an appropriate viral hepatitis research agenda (for relevant institutions) into national health policies and programmes
- Ensure adequate funds are allocated for research on viral hepatitis
- Establish a national database of all ongoing research relevant to the viral hepatitis programme, including drug trials and development of vaccine and diagnostic tools, and share this information both within the country and with other countries in the Region
- Set up a network of institutes engaged in research, such as national centres of excellence, academic institutions, and WHO collaborating centres, to support research relevant to national programmes, facilitate close collaboration between researchers and programme managers and promote actionable research
- Build/enhance institutional and individual capacity-building for preparing quality research proposals and conducting research that can be applied to prevention and control of viral hepatitis
- Promote research that determines influence of environmental, ecological and social factors on the epidemiology of viral hepatitis

## 10.4 Strategic framework for prevention and control

### WHO

- Advocate for the provision of safe water and proper sanitation
- Support country efforts to improve hygienic practices



- Provide technical assistance for preparedness, detection and response to outbreaks of viral hepatitis
- Provide technical assistance to conduct studies to determine the need for inclusion of hepatitis A vaccine in routine childhood immunization, and for persons with chronic liver disease
- Support countries to design and implement programmes for delivery of the dose of hepatitis B vaccine at birth
- Support countries in the formulation of policy to implement “catch-up” hepatitis B vaccination for adolescents
- Support countries in the formulation of national policy to extend hepatitis B vaccination to all health professionals and people in high-risk groups
- Support implementation of mandatory screening of all blood and blood products
- Support efforts to prevent iatrogenic transmission of hepatitis B and C

### Member States

- Intensify regular monitoring of quality water, take appropriate preventative measures in a timely manner and develop new approaches for improvement of people’s hygienic behaviour
- Develop a contingency plan and action for containment of HAV and HEV outbreaks and clearly define the role and responsibilities of the health sector and water and sanitation and community
- Conduct studies to determine the need for inclusion of hepatitis A vaccine in routine childhood immunization
- Formulate a hepatitis A vaccination policy for persons with chronic liver disease
- Design a programme for the delivery of the hepatitis B vaccine dose at birth, as part of the integrated package for maternal and neonatal care, if not yet implemented
- Start piloting a programme for delivery of the dose of hepatitis B vaccine at birth in selected districts, if not yet implemented
- Review the pilot programme and, based on results, modify the national strategy for hepatitis B immunization

- Study the appropriateness and feasibility of a national policy to extend hepatitis B vaccination to all children and adolescents under the age of 18 years, who have not been previously vaccinated, all health professionals and people considered as a high-risk group
- Review the current national policies on mandatory screening of blood and blood products for hepatitis B and C, using new highly specific and sensitive standardized diagnostic kits
- Monitor and enforce the safe injection programme in all health-care facilities
- Implement harm reduction interventions among injecting drug users
- Implement guidelines for safe practices for tattooing, piercing procedures and acupuncture

## 10.5 Strategic framework for education

### WHO

- Support countries' efforts to produce materials for general audience, emphasizing that everyone is affected; most affected individuals do not know they are "infected" and most do not have any visible symptoms
- Support countries' efforts to increase the knowledge of viral hepatitis among the general population and promote a healthy lifestyle among persons newly diagnosed or living with chronic hepatitis
- Support countries to improve and expand the knowledge of viral hepatitis among health-care and human service providers
- Use conferences and meetings as opportunities to promote detailed viral hepatitis awareness and service integration messages

### Member States

- Regularly mark 28 July as World Hepatitis Day and use it for mass campaigns for education and awareness across the country
- Aim to create a safe environment for accessing information, testing and care, particularly in rural and underserved communities

- For hepatitis B awareness, include messages about mother-to-child transmission and demographic groups with the highest rates of infection
- For hepatitis C awareness, include messages about blood transfusions and prior and past drug use.
- Educate the general public, to reduce unnecessary injections
- Facilitate training of water and sanitation staff on prevention of viral hepatitis
- Conduct training on prevention of viral hepatitis and integration of services for service providers working in the fields of HIV, STI, TB, alcohol and drug treatment, mental health, correctional facilities, immigrant health, refugee health, and others serving the at-risk population
- Conduct workshops/seminars for service providers and local health officials to share experiences integrating viral hepatitis prevention, education, testing, vaccination and care into their services

## 10.6 Strategic framework for medical care and treatment

### WHO

- Support countries in the establishment of the national referral centres for the care and treatment of viral hepatitis
- Support the establishment of networks among the national referral centres of Member States for medical care and treatment of viral hepatitis
- Support countries' efforts for the development of national capacities for medical care and treatment of viral hepatitis
- Support countries' efforts in development of standard procedures for the management of acute viral hepatitis
- Support countries' efforts in the development of guidance on counselling and support and care for infected individuals
- Support countries' efforts to evaluate current national treatment and care protocols for chronic hepatitis B, hepatitis C and HIV coinfections

- Support countries in adaptation and implementation of WHO consolidated treatment guidelines for the management of chronic hepatitis B and C and coinfections with HIV
- Support countries to conduct operational research for improvement of care and treatment of chronic HBV and HCV infections

### Member States

- Establish a national referral centre for medical care and treatment of viral hepatitis
- The national referral centre should be responsible for the coordination of medical care and treatment of viral hepatitis in the country
- The national referral centre should organize seminars, meetings and training in the field of care and treatment of viral hepatitis
- Develop standard procedures for the management of acute viral hepatitis
- Develop guidance on counselling, support and care for infected individuals
- Evaluate current protocols used for treatment of patients with chronic hepatitis B and C
- Participate in the field-testing and implementation of WHO consolidated treatment protocols for the management of chronic hepatitis B and C and HIV coinfections
- Conduct operational research for the improvement of care and treatment of chronic HBV and HCV infections

## Annex 1

## Summary of viral hepatitis transmission risk activities, prevention and treatment

Hepatitis	Modes of transition	Risk activities/factors	Prevention	Treatment options
A	<p>Ingestion of faecal matter, even in microscopic amounts, from:</p> <ul style="list-style-type: none"> <li>contaminated water, drinks and food prepared in unhygienic conditions</li> <li>close person-to-person contact with a person infected with hepatitis A</li> <li>sexual contact with a person infected with hepatitis A</li> </ul>	<ul style="list-style-type: none"> <li>Living in an area with high and intermediate hepatitis A endemicity</li> <li>Drinking unsafe water or other drinks and eating food using plates and kitchen utensils that are not properly washed</li> <li>Sexual contact with a person infected with hepatitis A</li> <li>Living with or caring for a person infected with hepatitis A</li> <li>Use of illegal drugs (injection or non-injection)</li> </ul>	<ul style="list-style-type: none"> <li>Hepatitis A vaccination</li> <li>Proper handwashing with soap after the use of toilets and changing nappies, and before preparing and eating food</li> <li>Drinking safe water using properly washed plates and kitchen utensils</li> <li>Immunoglobulin (in special conditions only)</li> </ul>	<p>Provide symptomatic and supportive treatment</p>

Hepatitis	Modes of transition	Risk activities/factors	Prevention	Treatment options
B	Contact with infectious blood, semen and other body fluids	<ul style="list-style-type: none"><li>• Birth from a mother infected with hepatitis B</li><li>• Sexual contact with a person infected with hepatitis B</li><li>• Multiple sexual partners</li><li>• Living with a STI</li><li>• Injection drug use</li><li>• Living with a person infected with hepatitis B</li><li>• Occupational exposure to blood</li><li>• Long-term haemodialysis</li><li>• Working in a health-care facility</li></ul>	<ul style="list-style-type: none"><li>• Hepatitis B vaccination</li><li>• Immunoglobulin</li><li>• Use of condoms for sexual intercourse</li><li>• Not sharing personal care items (e.g. razors, toothbrushes)</li><li>• Not sharing needles, syringes or drug paraphernalia (works)</li><li>• Ensure use of sterile equipment for any tattoo or body piercing</li><li>• Proper infection control in health-care settings and public safety work</li><li>• Screening blood and blood products for hepatitis B markers</li><li>• Reduce unnecessary injections</li></ul>	<ul style="list-style-type: none"><li>• For acute hepatitis B, provide supportive treatment</li><li>• For chronic hepatitis B, provide regular monitoring for signs of liver disease progression and consider antiviral medication</li></ul>

Hepatitis	Modes of transition	Risk activities/factors	Prevention	Treatment options
C	<p>Contact with infectious blood, primarily through:</p> <ul style="list-style-type: none"> <li>• sharing needles, syringes or drug paraphernalia</li> <li>• sexual contact with a person infected with hepatitis C</li> <li>• Birth from a mother infected with hepatitis C</li> <li>• Needle-stick or sharp instrument injuries</li> <li>• Tattooing/body piercing</li> </ul>	<ul style="list-style-type: none"> <li>• Current or past injection drug use</li> <li>• Receipt of blood or organs</li> <li>• Receipt of clotting factor concentrates</li> <li>• Long-term haemodialysis</li> <li>• Occupational exposure to blood</li> <li>• Birth from a mother infected with hepatitis C</li> </ul>	<ul style="list-style-type: none"> <li>• Not sharing needles, syringes or drug paraphernalia (works)</li> <li>• Use of condoms for sexual intercourse</li> <li>• Not sharing personal care items (e.g. razors, toothbrushes)</li> <li>• Ensure use of sterile equipment for any tattoo or body piercing</li> <li>• Proper infection control in health-care settings and public safety work</li> </ul>	<ul style="list-style-type: none"> <li>• For acute hepatitis C, provide supportive treatment and consider antiviral medication</li> <li>• For chronic hepatitis C, provide regular monitoring for signs of liver disease progression and consider antiviral medication</li> </ul>
E	<p>Ingestion of faecal matter, even in microscopic amounts, from:</p> <ul style="list-style-type: none"> <li>• contaminated water source</li> <li>• zoonotic transition from uncooked meat products</li> </ul>	<ul style="list-style-type: none"> <li>• Living in an area where hepatitis E infection is common</li> <li>• Drinking unsafe water or other drinks and eating food using plates and kitchen utensils that are not properly washed</li> <li>• Pregnancy</li> <li>• Consumption of uncooked meat products</li> </ul>	<ul style="list-style-type: none"> <li>• Improvement of sanitary and hygienic practices to eliminate faecal contamination of food and water</li> <li>• Provision of safe drinking water and proper disposal of sanitary waste</li> </ul>	<ul style="list-style-type: none"> <li>• Provide symptomatic and supportive treatment</li> </ul>

## Annex 2

# Surveillance of viral hepatitis

## Surveillance data

Surveillance data are used in a variety of ways by a broad base of researchers, clinicians, policy-makers and private industry. Regional and national surveillance systems provide population-based information that can be used to improve public health. They also offer an opportunity for public health interventions at the individual level, by linking infected people to appropriate care and support services. Overall, surveillance data are critical in estimating the incidence and prevalence of viral hepatitis infections and thus provide a basis for studying and understanding the diverse outcomes of the natural history of these infections (1–5).

## Outbreak detection and control

Accurate and timely surveillance data are necessary, to identify outbreaks of viral hepatitis in the general population and in health-care and community settings. The data can assist in recognizing and addressing breaches in infection control, and they can help to mitigate the size of outbreaks. There have been many outbreaks of HAV and HEV infections in the countries of the WHO South-East Asia Region associated with faecal contamination of food and water sources (6–11). Outbreaks of HBV and HCV infections have also been reported in health-care settings. They typically occurred in dialysis units, medical wards, nursing homes, surgery wards and outpatient clinics and resulted from breaches in infection control (12–20).

## Identifying infection

### Acute infection

#### *HAV infection*

The symptoms of HAV infection range from mild to severe, and can include fever, malaise, loss of appetite, diarrhoea, nausea, abdominal discomfort, dark-colored urine and jaundice. Not everyone who is infected will have all of the symptoms. Adults have



signs and symptoms of illness more often than children and the severity of disease and mortality increases in the older age groups. Infected children under 6 years of age do not usually experience noticeable symptoms, and only 10% develop jaundice. Among older children and adults, infection usually causes more severe symptoms, with jaundice occurring in more than 70% of cases. There is no evidence of chronic manifestation of HAV infection.

### **Standard case definition for acute HAV infection**

- *Clinical case definition:* an acute illness with (i) discrete onset of symptoms and (ii) jaundice, dark urine or elevated serum ALT levels, >200 IU/L
- *Laboratory criteria for diagnosis:* immunoglobulin M (IgM) antibody to hepatitis A virus (anti-HAV) positive
- *Case classification:* confirmed – a case that meets the clinical case definition and is laboratory confirmed

### **HBV AND HCV infection**

Several factors contribute to the difficulty in identifying acute HBV and HCV infections. Many newly acquired cases are asymptomatic, or they may have symptoms similar to those of other common illnesses and so do not prompt health-care providers to conduct serologic testing for HBV and HCV, or the serologic tests conducted are inadequate to distinguish between acute and chronic cases. About 90% of acute HBV infections in children under 5 years of age and 70% of HBV infections in adults are asymptomatic; 75–95% of acute HCV infections are asymptomatic (18, 19). Few infected patients seek care for the acute illness and there is a very high probability of underreporting, even when care is obtained. In addition, some persons with chronic HBV infection can experience a sudden increase in ALT that may be associated with jaundice or liver dysfunction. This change may be due to a variety of causes, including infection with another hepatitis virus, alcohol or drug use, or use of other medication or sudden reactivation of hepatitis B disease.

Classifying acute cases of hepatitis B and hepatitis C requires a complex integration of clinical data, positive and negative laboratory data, and prior or repeated testing. Many of the test results – for example, for ALT, IgM antibody to the hepatitis A virus, and IgM antibody to the hepatitis B core antigen (HBcAg) – are difficult for health departments to obtain.

### Standard case definition for acute HBV infection

- *Clinical case definition*: an acute illness with discrete onset of symptoms and jaundice or elevated serum ALT, >400 IU/L
- *Laboratory criteria for diagnosis*:
  - IgM antibody to hepatitis B core antigen (anti-HBc) positive, or HBsAg positive
  - IgM anti-HAV negative (if done)
  - IgM anti-HEV negative (if done)
- *Case classification*: confirmed – a case that meets the clinical case definition, is laboratory confirmed, and is not known to have chronic hepatitis B

### Standard case definition for acute HCV infection

- *Clinical case definition*: an acute illness with a discrete onset of any signs or symptoms consistent with acute viral hepatitis (e.g. anorexia, abdominal discomfort, nausea, vomiting), and either jaundice or serum ALT levels >400 IU/L
- *Laboratory criteria for diagnosis*: one or more of the following three criteria:
  - antibodies to hepatitis C virus (anti-HCV) screening test positive with a signal to cut-off ratio predictive of a true positive as determined for the particular assay as defined by Center for Disease Control and Prevention (CDC), USA; or
  - HCV RNA positive, and meets the following two criteria:
    - IgM antibody to hepatitis A virus (IgM anti-HAV) negative
    - IgM antibody to hepatitis B core antigen (IgM anti-HBc) negative
- *Case classification*: confirmed – a case that meets the clinical case definition, is laboratory confirmed, and is not known to have chronic hepatitis C

It is important to mention that currently used case definitions may miss a substantial fraction of clinically apparent acute cases of HBV infection because they lack clinical markers that could improve case identification and help to distinguish between acute and chronic cases.

Similarly, detection of acute hepatitis C can be challenging because no single case definition is either sensitive or specific for it. HCV seroconversion may be missed, and there is no IgM-based assay that reliably distinguishes acute hepatitis C from chronic hepatitis C, unlike the situation with HAV or HBV infection. Relatively low HCV RNA concentrations and more than one log fluctuation in HCV RNA concentration are features of acute HCV infection.

### **HEV infection**

Since cases of HEV infection are not clinically distinguishable from other types of acute viral hepatitis, diagnosis is made by blood tests that detect elevated levels of specific antibodies to hepatitis E in the body or by reverse transcriptase polymerase chain reaction (RT-PCR). Unfortunately, such tests are not widely available.

#### **Standard case definition for acute HEV infection**

- *Clinical case definition:* acute illness compatible with the following clinical description – jaundice, dark urine, anorexia, malaise, extreme fatigue and right upper abdominal quadrant pain and serum ALT levels >200 IU/L
- *Laboratory criteria for diagnosis:*
  - IgM antibody to HEV (anti-HEV) positive
  - detection of hepatitis E nucleic acid (e.g. PCR) in an appropriate clinical sample
- *Case classification:* confirmed – a case that meets the clinical case definition and is laboratory confirmed

In summary, the identification of acute hepatitis infection is inherently flawed because a vast majority of cases are asymptomatic and patients do not seek medical care or testing. Underreporting of diagnosed cases and misclassification of reported cases seriously limit the accuracy of data on cases of acute viral hepatitis collected by surveillance programmes. Thus, the estimates of the incidence of acute hepatitis in the countries of the WHO South-East Asia Region are based solely on symptomatic cases.

The majority of those cases may be missing from the surveillance system because of poor access to health care, underreporting and misclassification. Taken together, published surveillance summaries of reported cases of acute viral hepatitis substantially underestimate the number of cases. Ultimately, these summaries may give misleading impressions of the incidence of disease to policy-makers and programme planners.

Chronic HBV and HCV infections

HBC and HCV infections are largely asymptomatic and most people do not receive a diagnosis until the infection is chronic.

HBV

HBV infections become chronic in over 90% of infants who are infected at birth or in the first year of life and in 30% of children who are infected at the age of 1–5 years (22). Although HBsAg is detectable within 4–10 weeks after infection, it is only indicative of chronic HBV infection if it persists for more than 6 months. An accurate diagnosis of chronic hepatitis B may therefore require the reporting of multiple serologic markers at more than one time (23). For the purpose of disease surveillance, it can be challenging for health departments to obtain the complete laboratory results that are necessary to classify a chronic hepatitis B case according to standard HBV case definition. In general, a full hepatitis B panel (including any negative results for IgM anti-HBc) is required, or two HBsAg results at least 6 months apart. Interpretation of HBV markers is summarized in Table 9.

Table 9: Interpretation of HBV markers

Markers	Infection		
	Acute	Chronic	Past
HBsAg	+	+	–
HBeAg	+ early, then –	+/–	–
Anti-HBsAg	–	–	+
Anti-HBc IgM	+	–	–
Anti-HBc IgG	+	+	+
Anti-HBe	– early, then +	+/–	+
HBV DNA	+ early, than –	+/–	–
ALT	Increased (marked)	Increased (mild to moderate)	Normal

## Standard case definition for chronic HCV infection

- *Clinical description:* persons with chronic HBV infection may have no evidence of liver disease or may have a spectrum of disease ranging from chronic hepatitis to cirrhosis or liver cancer; persons with chronic infection may be asymptomatic
- *Laboratory criteria:*
  - IgM antibodies to anti-HBc negative and a positive result on one of the following tests:
  - HBsAg, HBeAg, HBV DNA; or
  - HBsAg positive or HBV DNA positive or HBeAg positive two times, at least 6 months apart (any combination of these tests performed 6 months apart is acceptable)
- *Case classification:*
  - confirmed – a case that meets either laboratory criteria for diagnosis
  - probable – a case with a single HbsAg-positive or HBV-DNA-positive or HbeAg-positive laboratory result when no IgM anti-HBc results are available

It is important to mention that multiple laboratory tests indicative of chronic HBV infection may be performed simultaneously on the same patient specimen as part of a “hepatitis panel”. Testing performed in this manner may lead to seemingly discordant results, e.g. HBsAg negative and HBV DNA positive. For the purposes of this case definition, any positive result among the three laboratory tests mentioned above is acceptable, regardless of other testing results. Negative HBeAg results and HBV DNA levels below the positive cut-off level do not confirm the absence of HBV infection.

## HCV

In adults, about 15–25% of acute HCV infections resolve spontaneously (24). That may increase to about 45% in children and young adults (25). The presence of HCV RNA is generally detected within 1 week of infection (26), but antibodies to HCV (anti-HCV) can be detected in only 50–70% of infected persons at the onset of symptoms. This increases to more than 90% after 3 months. A chronic infection is characterized by the

persistent presence of HCV RNA for at least 6 months. Typically, when a patient presents for HCV testing, the first test that is conducted is for the presence of anti-HCV. This test is generally an enzyme immunoassay (EIA). A repeatedly reactive EIA is followed by a more specific assay to detect viraemia, such as testing for HCV RNA.

However, all confirmed anti-HCV test results should be followed by a test for the presence of HCV RNA (27). The difficulty in identifying chronic cases often revolves around the need for two separate tests (or other supplemental antibody tests) and the 6-month time frame required for a diagnosis of chronic HCV infection. Many infected people are tested at public or nonclinical testing sites such as drug-treatment facilities or sites for testing for HIV or STIs, or by community-based organizations that conduct only the less expensive anti-HCV tests. Persons tested at those sites might not have access to an HCV RNA test, or the laboratory conducting the initial EIA test might not routinely test for HCV RNA when an EIA has been positive. This process leads to incomplete diagnoses and inaccurate reporting of the number of chronic cases.

### **Standard case definition for chronic HCV infection (past or present)**

- *Clinical description:* most HCV-infected persons are asymptomatic; however, many have chronic liver disease, which can range from mild to severe, including cirrhosis and liver cancer
- *Laboratory criteria for diagnosis:*
  - anti-HCV positive (repeat reactive) by EIA, verified by an additional more specific assay (testing for HCV RNA); or
  - nucleic acid test for HCV RNA positive; or
  - anti-HCV screening test positive with a signal to cut-off ratio predictive of a true positive as determined for the particular assay
- *Case classification:*
  - confirmed – a case that is laboratory confirmed and that does not meet the case definition for acute hepatitis C
  - probable – a case that is anti-HCV positive (repeat reactive) by EIA and has ALT or serum glutamic-pyruvic transaminase (SGPT) values above the upper limit of normal, but the anti-HCV EIA result has not been verified by an additional more specific assay, or the signal-to-cut-off ratio is unknown

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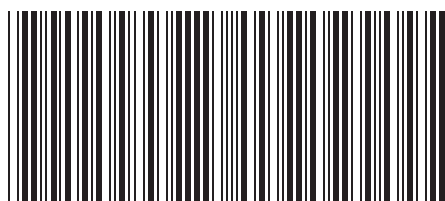


Viral hepatitis is a serious public health problem worldwide, as well as for the Member States of the WHO South-East Asia Region. The complexity of hepatitis disease lies in the existence of different types of viruses. Hepatitis A and E are foodborne and waterborne infections that cause millions of cases of acute illness every year. Hepatitis B, C, and D are spread in a number of ways, namely by receiving unscreened blood and blood products, sexual contact, mother-to-child transmission during birth, or through use of contaminated medical equipment. Hepatitis B and C have a greater health burden and a high mortality related to chronic infection, which in turn can lead to cirrhosis and liver cancer. Considering the importance of prevention and control of viral hepatitis, the WHO Regional Office for South-East Asia, together with active participation of the representatives of the Member States has developed a regional strategy for prevention and control of viral hepatitis. The goal of the strategy is to implement policies, programmes and interventions to interrupt transmission and reduce the incidence and the socioeconomic consequences of viral hepatitis in the Region.



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