

# Achieving WHO target of HCV control in Hong Kong: challenges and strategies

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**Abstract:** With the introduction of effective directly acting antiviral agents (DAAs) therapy, control and elimination of hepatitis C virus (HCV) infection is becoming a feasible goal. In Hong Kong, HCV prevalence in general population is 0.3%-0.5% over the past decades. However, like other high-income areas/countries, high prevalence of HCV infection has been found in several population groups, such as people who inject drugs (PWID), patients undergoing dialysis, and human immunodeficiency virus infection and acquired immunodeficiency syndrome (HIV/AIDS) patients. Based on the epidemiological study using data retrieved from the Hong Kong HCV Registry from January 2005 to March 2017, the estimated territory-wide diagnosis rate and treatment rate of HCV infection were only 50.9% and 12.4%, respectively. Although these rates were comparable to many developed countries/areas, the performances remained substantially below 90% and 80%, the 2030 targets proposed by World Health Organization (WHO). In recognition of the challenges, the Hong Kong Government set up the Steering Committee on Prevention and Control of Viral Hepatitis (SCVH) which formulated the *Hong Kong Viral Hepatitis Action Plan 2020-2024*. The *Action Plan* adopts four key strategies, as described in the WHO framework for global action, namely, awareness, surveillance, prevention and treatment. With the effective implementation of the *Action Plan*, especially in targeted screening of high-risk populations and more generalized use of the highly efficacious DAAs for all diagnosed HCV subjects, the goals of reducing HCV transmission and HCV-related morbidity and mortality can be achieved in Hong Kong by 2030.

**Keywords:** HCV, prevention, treatment, elimination, Hong Kong

## Introduction

Hepatitis C virus (HCV) is a small, enveloped, single stranded RNA virus identified in 1989 and is transmitted mainly through exposure to contaminated blood or blood products (1,2). As one of the major causes of liver-related morbidity and mortality, including liver cirrhosis and hepatocellular carcinoma (HCC), chronic HCV infection is becoming an important public health burden, with around 71 million infections worldwide and at least 400,000 deaths per year (3-5). Currently, there is still no effective vaccine for the prevention of HCV infection (6).

Over the past dozen years, the mainstay treatment for patients with HCV infection was the combination of weekly subcutaneous injections of pegylated interferon (PegIFN) and daily oral ribavirin (RBV). This treatment required 24-72 weeks and was accompanied by a wide variety of side effects and less than 60% of patients can achieve the sustained virologic response (SVR) (7-9). The development of directly acting antiviral (DAA)

agents has revolutionised HCV treatment since 2014. Compared to the PegIFN/RBV regimen, DAA therapy is of shorter duration (8-24 weeks) and achieves over 90% SVR rate. It is also well tolerated and suitable for patients with former contraindications to PegIFN/RBV therapy, such as patients with decompensated cirrhosis or significant comorbidities (10-12). The pan-oral, IFN-free DAAs regimens with or without RBV have recently been recommended as the first-line therapy for HCV infection in clinical practice guidelines endorsed by different academic societies (13-16).

Meanwhile, in the light of these more efficacious treatment options, the World Health Organization (WHO) proposed to eliminate HCV as a public health threat, targeting a diagnosis rate of 90% of total infections, a 90% decrease in new infections and a 65% decrease in liver-related mortality by 2030 as compared with the baseline in 2015 (17). To realize these targets, several significant barriers should be overcome, including knowledge and awareness of viral hepatitis, identification of undiagnosed individuals, linkage to

continued care, and prevention of the occurrence of new cases or re-infection.

In this review, we summarize the current status of HCV epidemiology, diagnosis and treatment in Hong Kong, and outline the strategies formulated by the Hong Kong government for achieving the WHO goal of eliminating viral hepatitis as a major public health threat by 2030.

**Epidemiology of HCV infection in Hong Kong**

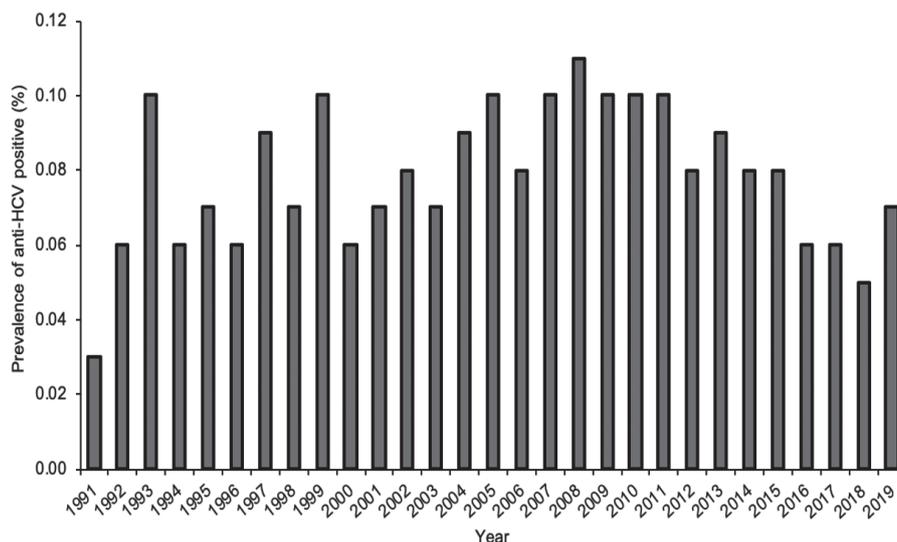
*Prevalence of HCV*

In contrast with high prevalence of hepatitis B virus (HBV) infection in Hong Kong, HCV infection is an uncommon occurrence among the local general population. One study of 382 individuals who attended a health exhibition in 1988 found that the prevalence of anti-HCV positivity was 0.5% (18). A community-based, territory-wide epidemiological study recruited 10,256 participants from February 2015 to July 2016, and found that overall anti-HCV positivity was 0.5% and the prevalence of viraemic HCV infection was 0.3% (19). Meanwhile, data from new blood donors in Hong Kong Red Cross Blood Transfusion Service, a major source of HCV epidemiological information, showed that HCV prevalence in adolescents and young adults ranged between 0.03% and 0.11% since the implementation of anti-HCV screening in 1991 (Figure 1). Among 29,332 new blood donors screened in 2019, anti-HCV was more commonly detected in subjects aged over 40 years as compared to those aged below 40 years (0.19% vs. 0.04%), and males were more commonly infected than females (0.10% vs. 0.05%) (20).

Before 1990s, HCV was infected mainly through transfusion with contaminated blood or blood products. With the introduction and implementation of anti-HCV

screening for blood donations since 1991, the risk of transfusion-transmitted HCV infections has decreased to a very low level in Hong Kong (21). Transfusion-transmitted HCV infections are mainly found in patients requiring frequent blood or blood product transfusions, such as haemophilia patients. In high-income areas/countries, most HCV transmission has been found among PWID (22). From local studies published in the early 1990s, it was shown that anti-HCV was more commonly found in PWID (66.8%) and haemodialysis patients (4.6%) (18). An HCV seroprevalence study conducted in 2006 in methadone clinics, showed a 85% prevalence rate of anti-HCV seropositivity in this community (23). More recent studies involving PWID recruited at their gathering places also gave a similar figure of anti-HCV prevalence of 81.7% among 622 subjects in 2011 and 76.4% among 664 subjects in 2014, respectively (24,25). Among these subjects, injection duration, current or recent injections, sharing of injecting needles and concomitant use of other drugs, such as midazolam, were identified as the independent factors associated with HCV infection. In the New Life New Liver Project conducted between 2009 and 2018, 73.4% of 365 subjects participating in a targeted screening and assessment program for ex-PWID, were found to be anti-HCV positive (26).

HIV/AIDS patients are another population disproportionately affected by HCV infection in Hong Kong. Among 4416 new HIV/AIDS patients attending the Integrated Treatment Centre of Centre for Health Protection from 2000 to 2019, 385 (8.7%) tested positive for anti-HCV, and the prevalence rate appeared to be higher in male than female patients (9.4% vs. 4.1%) (20). HIV/HCV coinfection was found in 1.5-6.0% of HIV/AIDS patients infected through sexual contact, as compared with 97% of those patients infected through drug injection. Among those heterosexual HIV-infected



**Figure 1. Prevalence of anti-HCV positive in new blood donors from 1991 to 2019 in Hong Kong** (Date source: Hong Kong Red Cross Blood Transfusion Service, Hong Kong Special Administrative Region, China).

male patients without history of intravenous drug use, only 2.5% were anti-HCV positive (20).

### HCV Genotypes

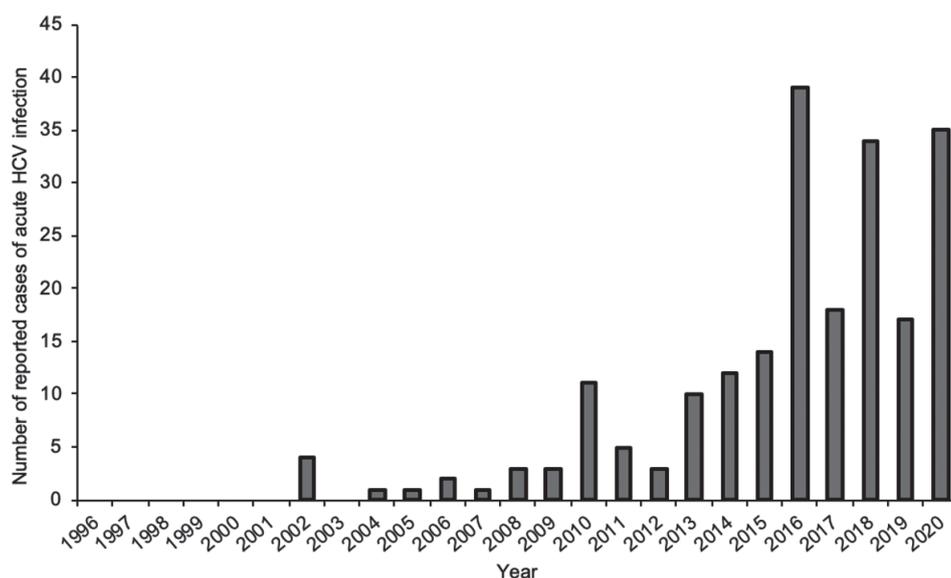
HCV is an enveloped, positive-strand RNA virus with extensive genetic heterogeneity, and has been classified into 7 major genotypes and over 75 subtypes with broad distribution in different geographical distributions (27). In contrast to western countries/regions where HCV genotype 1a is the most prevalent, HCV infections in Hong Kong are predominately caused by genotype 1b and 6a (28). In an early study involving 212 viraemic blood donors from 1991 to 1994, genotype 1b and 6 were detected in 58.8% and 27.0%, respectively (29). In a recent comprehensive population-based epidemiological study, the prevalent HCV genotype was genotype 1 (48.8%), followed by genotype 6 (33.6%), genotype 3 (10.8%) and genotype 2 (3.2%) among 2699 anti-HCV positive patients from all public hospitals in Hong Kong between January 2005 and March 2017 (30). While in HIV/HCV co-infected patients, genotype 3 is the most common (27.2%), followed by genotype 1a (14.8%), genotype 1b (11.1%) and genotype 6 (11.1%) (30).

### Current challenges and strategies in controlling HCV infection in Hong Kong

Although much has been done to prevent and control HCV infection and keep the prevalence rate low over the past decades in Hong Kong, a higher number of acute HCV infections had been reported annually in the past ten years as compared with the decade before (Figure 2) (20). Hong Kong is an international city with high population mobility, and people may get HCV infection in other countries/areas where effective

screening and control of HCV infection might not have been implemented and achieved (21). Certain misconceptions of HCV infection are also widespread in the local community, such as the disease cannot be cured, or the disease is relatively benign because most of the patients with HCV infection are asymptomatic in the early phase. A retrospective analysis of untreated HCV-infected patients from 2000 to 2009 found that 31.9% of 138 patients declined treatment due to patients' preference (31). Based on the recent epidemiological study using data retrieved from the Hong Kong HCV Registry which covers up 94% of all secondary and tertiary care services in Hong Kong, a total of 11,309 patients who tested positive for anti-HCV were identified from January 2005 to March 2017 (30). Among these patients, only 2201 were found to have received antiviral treatment. Given a population of 7.4 million people and assuming a prevalence of 0.3% HCV infection with a viremic rate of 80% in Hong Kong, the estimated territory-wide diagnosis rate and treatment rate were only 50.9% and 12.4%, respectively. Although these rates were comparable to many developed countries/areas, the performance remained substantially below the 2030 targets of 90% and 80%, proposed by WHO.

Based on the hepatitis elimination initiative of the WHO, it is critical to identify HCV infected individuals to start antiviral therapy, avoid further transmission and the occurrence of new cases (4). Traditionally, HCV screening starts with testing the antibodies against HCV (anti-HCV) with immunoassay and then viral load quantitation using a polymerase chain reaction-based assay for subjects with positive anti-HCV results. This two-step process requires multiple visits and may take several days or weeks, leading to delayed diagnosis and increased risk of losing the patient to follow-up treatment (32). With the development of point-of-care



**Figure 2. Number of reported cases of acute HCV infection from 1996 to 2020 in Hong Kong** (Date source: Centre for Health Protection, Department of Health, Hong Kong Special Administrative Region, China).

(POC) and rapid diagnostic tests (RDT) which can offer results in minutes, rapid screening, confirmation of diagnosis and treatment initiation in the same clinic visit are possible nowadays.

Before 2014, PegIFN/RBV therapy was the mainstay treatment of patients with HCV infection. However, many patients with HCV infection declined the treatment due to the long treatment duration and associated adverse effects. It was noted that of 1,533 patients in consideration for PegIFN/RBV therapy, 16.1% refused this regimen while 17.2% did not get the treatment due to contraindication (30). With the development of DAAs, the treatment paradigm for HCV infection has been revolutionised since 2014. In comparison with traditional IFN-based therapy, DAAs are associated with high SVR (> 90%), shorter treatment duration (8-24 weeks), and much fewer side-effects. However, the high price of DAA therapy may prohibit its widespread use (33-35). In Hong Kong, due to a limited health-care budget and lack of comprehensive insurance coverage schemes, DAAs are not universally prescribed for every patient with HCV infection. Risk stratification is the strategy adopted by the Hospital Authority to prioritize those patients with advanced liver fibrosis (F3) or cirrhosis (F4), to receive subsidized DAA treatment.

In recognition of these service gaps, the Hong Kong Government announced in the 2017 Policy Address setting up a steering committee to formulate strategies to prevent and control viral hepatitis effectively. After reviewing local and international trends and new developments in the prevention and control of viral hepatitis, the committee formulated the *Hong Kong Viral Hepatitis Action Plan 2020-2024* in October 2020, providing a detailed strategic process for controlling HCV infection and reducing the public health burden in Hong Kong (36). The *Action Plan* adopts four key strategies, as described in the WHO framework for global action, namely, awareness, surveillance, prevention and treatment, to eliminate HCV infection in Hong Kong (Table 1).

### Awareness

Lack of knowledge and awareness about HCV infection probably contributes to continued HCV transmission and missed prevention, early diagnosis and medical care opportunities (37). As described in the *Action Plan*, VHCO has been promoting public awareness through various channels, including, telephone hotline, internet, printed materials, health talks for the public, *etc.* A website ([www.hepatitis.gov.hk](http://www.hepatitis.gov.hk)) has been revamped to provide essential and up-to-date information on viral hepatitis by VHCO in early 2020. Roving exhibitions on viral hepatitis with different yearly themes of the awareness campaign are held on World Hepatitis Day each year. Meanwhile, professional training programs with the knowledge-attitude-practice (KAP) assessment for healthcare workers of different specialties are conducted in phases. Education on safe injection and safer sex practices for prevention of HCV infection is being integrated with the HIV prevention program, while standardized training and education materials on HCV infection for service providers of PWID is also developed. More importantly, the awareness campaign should emphasize that HCV is not a benign disease, which can potentially lead to liver cancer and liver failure, but the disease is curable nowadays.

### Surveillance

As indicated by the *Action Plan*, the present surveillance system has some limitations, including under-reporting, seroprevalence data limited to specific subgroups, and artificial variation in incidence. A set of local indicators for monitoring and evaluation of HCV elimination strategies, including the prevalence of chronic HCV infection, people living with HCV diagnosed, treatment initiation and cure for patients with HCV infection, incidence of HCV infection, and deaths attributable to HCV infection, have been adopted to enhance the current surveillance system. Meanwhile, the Population Health Survey (PHS), a territory-wide survey with

**Table 1. The action plan for eliminating HCV epidemic in Hong Kong**

Key strategies	Contents
Awareness	<ul style="list-style-type: none"> <li>- Awareness campaign for the general population</li> <li>- Professional training for healthcare workers</li> <li>- Education targeting at-risk populations, patients and their service providers</li> <li>- Building a supportive environment</li> </ul>
Surveillance	<ul style="list-style-type: none"> <li>- Ongoing surveillance from notification system for acute and chronic HCV infection</li> <li>- Development of local indicators for monitoring and evaluation of the HCV elimination strategies</li> </ul>
Prevention	<ul style="list-style-type: none"> <li>- Reduction of risk and disease burden in vulnerable populations</li> <li>- Prevention of healthcare-related transmission of HCV</li> </ul>
Treatment	<ul style="list-style-type: none"> <li>- Promotion of HCV testing in people who inject drugs</li> <li>- Micro-elimination of HCV in targeted populations</li> <li>- Expansion of access to DAAs for HCV</li> </ul>

two components, namely household questionnaire survey and health examination, is being conducted during 2020-2021. It will cover the land-based non-institutional population aged 15 or above for the household questionnaire survey and a subsample of respondents aged between 15 and 84 for health examination. It will provide a representative and detailed analysis of the latest prevalence of chronic HCV infection in the general population, as well as the proportion of patients with chronic HCV infection who have been diagnosed, treated and cured. Clinical data from Health Authority will be the main data source for treatment initiation and cure for HCV patients as the majority of local populations are receiving outpatient and inpatient services for viral hepatitis in public hospitals of the Health Authority. Hopefully, this will significantly improve the 12% HCV treatment rate among diagnosed subjects reported in the territory-wide population-based study of chronic HCV infections in 2018 (30).

#### *Prevention*

Due to lack of a safe and effective vaccine, controlling practices known to spread HCV and curing patients with HCV infection should be taken as the prevention measures. In Hong Kong, the current blood safety strategies based on voluntary blood donations and quality-assured screening program can prevent transmission of HCV effectively. Patients potentially infected with HCV through contaminated blood or blood procedures before the implementation of anti-HCV screening for blood donors in 1991 are being traced, investigated and treated by Health Authority. Meanwhile, infection control training on Standard Precautions, such as aseptic technique, proper sharps handling and management of needlestick injury or mucosal contact, is being provided to healthcare workers on a regular basis, with an aim to reduce their chance of acquiring or passing on infections of HCV, through occupational exposure. On the other hand, condom programming and a harm reduction approach are needed to be intensified due to the emergence of sexually acquired HCV infection in HIV-positive MSM. The possibility that sexually acquired HCV crosses to HIV-negative MSM should also be scrutinized.

#### *Treatment*

Curing chronic HCV infection has been demonstrated to have an immense benefit not only for the patients but also society (38-40). With the gradual expansion of DAA therapy from patients with advanced fibrosis or cirrhosis who were contraindicated or intolerant to conventional PegIFN/RBV therapy to all HCV patients regardless of their disease severity in the fourth quarter of 2021 stated in the *Action Plan*, the remaining

obstacles to treatment are identification of undiagnosed HCV patients and linkage to continued care and treatment. Universal screening for anti-HCV is not cost-effective due to the low prevalence of HCV infection in Hong Kong. However, several population groups with high prevalence of HCV infection, such as patients undergoing dialysis and HIV-positive patients, will be targeted for screening and treatment to achieve micro-elimination in these well-defined populations. PWID is another priority population for enhancing prevention, testing, linkage to care, treatment and follow-up care. A policy initiative to promote HCV screening and treatment in PWID, who are attending methadone clinics or are under custody of Correctional Services Department, has been established. Perhaps, point-of-care and rapid diagnostic tests can be offered to PWID attending methadone clinics along with educational information about HCV transmission through contaminated injection equipment. Currently, there are around 5,200 people registered with methadone clinics with an average 3,900 daily attendance. A pilot program involving selected methadone clinics is being carried out to test the feasibility and assess the acceptance of HCV testing among PWID. The information gained from the pilot program can also help better characterize the barriers to HCV testing and care, and devise strategies to overcome them.

The implementation of the above *Action Plan* will be monitored and evaluated regularly through different targets and indicators to drive progress towards the WHO 2030 goals of eliminating HCV infection in Hong Kong.

#### **Conclusions**

In Hong Kong, the estimated HCV prevalence in general population is 0.3%-0.5%, prevailing in several specific populations, including PWID, patients undergoing dialysis and HIV/AIDS patients. However, our territory-wide diagnosis rate and treatment rate are still substantially below the 2030 WHO targets of viral hepatitis elimination. To realize the elimination target, four key strategies including awareness, surveillance, prevention and treatment have been adopted in the *Hong Kong Viral Hepatitis Action Plan 2020-2024*. With the implementation of the *Action Plan*, especially in targeted screening approaches on high-risk populations and more generalized use of the highly efficacious DAAs for all diagnosed HCV subjects, the goals of reducing HCV transmission and HCV-related morbidity and mortality to the WHO targets can be achieved in Hong Kong by 2030.

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