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Micro-elimination of hepatitis C in people who inject drugs

Introduction

Hepatitis C is a significant global disease burden, with an estimated 58 million people worldwide chronically infected with hepatitis C virus (HCV) in 2019 [1]. Most HCV infections are acquired through contact with blood of an infected person. Common transmission routes include sharing needles, syringes or other equipment for injecting drugs, reusing inadequately sterilised medical equipment, transfusion of unscreened blood and blood products and occupational exposure to blood or body fluid with HCV. Acute HCV infections are usually asymptomatic, and most do not cause life-threatening disease. However, only 36.1% (95% confidence interval (CI): 23.5% - 50.9%) of infected individuals could achieve spontaneous clearance of HCV within 12 months following acute infection [2] and chronicity following HCV infection is common. If left untreated, chronic HCV infection can lead to cirrhosis, hepatocellular carcinoma (HCC) and even death. In 2019, there were 290 000 people dying from HCV-related causes [1].

Global epidemiology of HCV infection in PWID

The hepatitis C epidemic and injecting drug use (IDU) are two interconnected public health issues, in the context of the disease morbidity and mortality. The World Health Organization (WHO) estimated that current IDU accounted for 23% of new HCV infections globally, and 8% of current HCV infections were among people who inject drug (PWID). Of all the deaths from cirrhosis and HCC due to HCV infection, 31% were attributable to a lifetime history of IDU [3].

Systematic reviews published in 2011 found that 37 out of 77 countries had an estimated midpoint anti-HCV prevalence exceeding 60% among PWID [4]. The latest systematic review covering 98 countries gave an estimated number of anti-HCV-positive PWID at 8.2 million (95% uncertainly interval (UI): 4.7 – 12.4 million), corresponding to an anti-HCV prevalence at 52.3% (95% UI: 42.4% – 62.1%) [5].

In the Global Burden of Disease Study 2013, IDU was estimated to cause 39.1% of disability-adjusted life-years (DALYs) attributable to HCV, much higher than the DALYs due to human immunodeficiency virus (HIV) (4.0%) and hepatitis B virus

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(HBV) (1.1%) [6].

In addition, PWID infected with HCV are at increased risk of both liver-related and all-cause mortality [7, 8], reflecting a combined role of IDU, low socio-economic status, poor access to health care and environmental factors [9].

Local situation of HCV infection in PWID

IDU is also an important route of HCV acquisition in Hong Kong. An HCV seroprevalence study in 2006 conducted in methadone clinics targeting PWID found that the prevalence of anti-HCV among the 567 PWID participants recruited was 85% (95% CI: 82.5% - 88.3%) [10]. Two other studies in 2010s, involving PWID recruited at their gathering places, gave a similar figure of anti-HCV prevalence at 81.7% (95% CI: 78.6% - 84.7%) among 622 subjects in 2011 [11] and 76.4% (95% CI: 73.1% - 79.6%) among 664 subjects in 2014 [12] respectively. Injection duration, current or recent injection, ever sharing injecting equipment and concomitant use of other drugs, such as midazolam, were independent factors associated with HCV infection in these studies. In the recent New Life New Liver Project, which provided targeted HCV screening and education to ex-PWID in the community, 73% of 365 subjects screened were anti-HCV positive. The number needed to screen to detect one patient with positive anti-HCV was 1.4 (95% CI: 1.3 - 4.6) [13].

The major public health burden from HCV infection in PWID is signified by the stark contrast to the low prevalence of anti-HCV in the general population at 0.5%, as found in a territory-wide study conducted in 2015 - 16 [14]. A detailed review of 1533 anti-HCV-positive patients from two public hospitals (Princes of Wales Hospital and Queen Elizabeth Hospital) between January 2005 and March 2017 found that most of the HCV infections were acquired through IDU (36.7%), followed by blood product transfusion (30.0%) and unknown route (27.2%) [15]. Notably, since the institution of blood donor screening for HCV in 1991, the risk of transfusion-transmitted HCV infection has decreased to a very low level [16].

Global strategies in prevention and control of hepatitis C

In the past decade, the development of highly effective treatment regimens, including direct-acting antiviral medicines, has revolutionised the treatment of HCV infection and provide an unprecedented opportunity to end the hepatitis C epidemic as a major public health threat. In 2016, WHO published the first *Global health sector strategy on viral hepatitis, 2016 – 2021 (GHSS 2016 - 2021)* and set clear impact targets at 80% reduction in incidence and 65% reduction in mortality for

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HCV infection by 2030, as compared with the baseline number in 2015. Service coverage targets were set at 90% and 80% for diagnosis rate and treatment coverage in 2030 respectively, while other targets on blood safety, safe injections and harm reduction were also established [17].

In June 2021, WHO developed an interim guidance for countries and other stakeholders seeking validation of elimination of viral hepatitis as a public health problem [18]. The guidance suggests the use of absolute impact targets to validate elimination at the national level (instead of, although equivalent to, the relative reduction targets originally defined in the *GHSS 2016 - 2021*) in combination with a set of programmatic targets. For HCV infection, the main impact targets for measuring elimination include (a) an absolute annual HCV incidence of ≤ 5 per 100 000 persons and of ≤ 2 per 100 PWID and (b) an HCV-related annual mortality rate of ≤ 2 per 100 000 persons. The use of absolute incidence target involving PWID could indeed reflect the significance of epidemic dynamics driven by sharing of needles, syringes and drug paraphernalia among PWID in most countries.

Micro-elimination of HCV infection

To achieve the goal of global elimination of HCV infection as a public health threat, International Liver Foundation of the European Association for the Study of the Liver recommended a micro-elimination approach, which refers to targeted elimination of HCV infection in well-defined populations. It is a strategy to achieve elimination incrementally through initiatives that eliminate hepatitis C for defined segments of the population, such as within settings, geographic areas, subpopulations and age cohorts [19]. Targeting smaller and clearly delineated HCV risk groups allows faster and more efficient delivery of interventions [20] and enables stakeholders who are the most knowledgeable about specific populations to engage with each other [21]. The selection of targeted groups for micro-elimination initiatives should be based on the hepatitis C epidemiology and health context of different countries and subnational areas. Candidate populations for micro-elimination due to their higher burden of HCV infection may include haemodialysis recipients, HIV/HCV co-infected people, PWID and prisoners.

Prevention and control of hepatitis C in PWID in Hong Kong

In October 2020, the Government launched the *Hong Kong Viral Hepatitis Action Plan 2020 – 2024* (“the Action Plan”), which is the first blueprint formulated to reduce the burden of both chronic hepatitis B and C [22]. The Action Plan sets out

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priority actions in four strategic axes, namely raising awareness, enhancing surveillance, promoting prevention and expanding access to treatment. The specific actions for prevention and control of hepatitis C, including both current practice and new initiatives, are described as follows, with a focus on those targeting PWID.

Reduce risk and disease burden in PWID

In 1976, an extensive network of methadone treatment programme (MTP) was launched, as part of its multi-pronged strategy on drug abuse treatment, aiming to provide a readily accessible, legal, medically safe and effective alternative to continued illicit self-administration of opiate drugs [23]. Since the local emergence of HIV in the mid-1980s, the objectives of MTP were extended to reduce intravenous drug use and needle sharing and thereby prevent the spread of diseases like HIV/AIDS, viral hepatitis and other blood-borne diseases. With a high coverage, MTP has contributed to keeping a relatively low HIV prevalence among PWID [24]. MTP will continue as the main harm reduction strategy adopted in Hong Kong. The network of methadone clinics affords the opportunity to engage PWID for health education, prevention and control of hepatitis C.

Expansion of access to direct-acting antivirals for HCV

Most HCV infection can now be cured by direct-acting antivirals (DAA). Since 2018, WHO has recommended offering treatment to all individuals aged 12 or above with HCV infection, irrespective of disease stage, as well as the use of pan-genotypic DAA regimens for the treatment of persons with chronic HCV infection aged 18 years and above [9]. DAA regimens are highly effective and well tolerated, and take a much shorter time to complete (8 -12 weeks for adults without cirrhosis) than that for interferon-based treatment.

Sustained virological response (SVR) is an indicator of treatment success and it occurs when blood test shows no detectable HCV RNA in 12 weeks after treatment. Patients having achieved SVR after treatment are considered as cured, and will not transmit the virus to others.

As summarised in a systematic review, there are at least two DAA regimens available for each of the six HCV genotype infection, which could generally achieve high SVR rates (Genotype 1: >95%, genotype 2, 4, 5 and 6: >92%) [25]. The pooled proportion achieving SVR at 12 weeks post-treatment was found to exceed 94% for

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all pan-genotypic regimens across HCV genotypes 1, 2 and 4, while a lower rate of SVR was observed for genotype 3 HCV infection, ranging between 65% and 89% [26].

Despite the high effectiveness, the high cost of DAA regimens used to pose a challenge on treatment accessibility. Prior to 2019, only patients with advanced fibrosis or cirrhosis who were contraindicated or intolerant to conventional interferon-based therapy were eligible for subsidised DAA treatment in Hong Kong.

Since October 2020, the Hospital Authority drug formulary indication for DAA treatment has been expanded to cover all hepatitis C patients, irrespective of their stage of liver fibrosis. This initiative might allow a shortened interval between diagnosis and treatment initiation, facilitating the linkage to care for individuals diagnosed with HCV infection. An earlier cure of HCV infection not only brings clinical benefits for individual health, but also potentially infers “treatment as prevention” impact for public health by reducing the number of infected individuals in the community, especially among PWID [27].

Promotion of HCV testing in people who inject drugs

WHO recommends offering serological testing for HCV antibody (anti-HCV) with linkage to prevention, care and treatment services to PWID who are regarded as one of the most affected populations. Following a reactive HCV antibody serological test result, a quantitative or qualitative RNA nucleic acid testing (NAT) is recommended as the preferred testing strategy to diagnose viraemic infection (Figure 1). For some with ongoing risk of acquisition or reinfection, periodic re-testing using HCV NAT should also be considered [28].

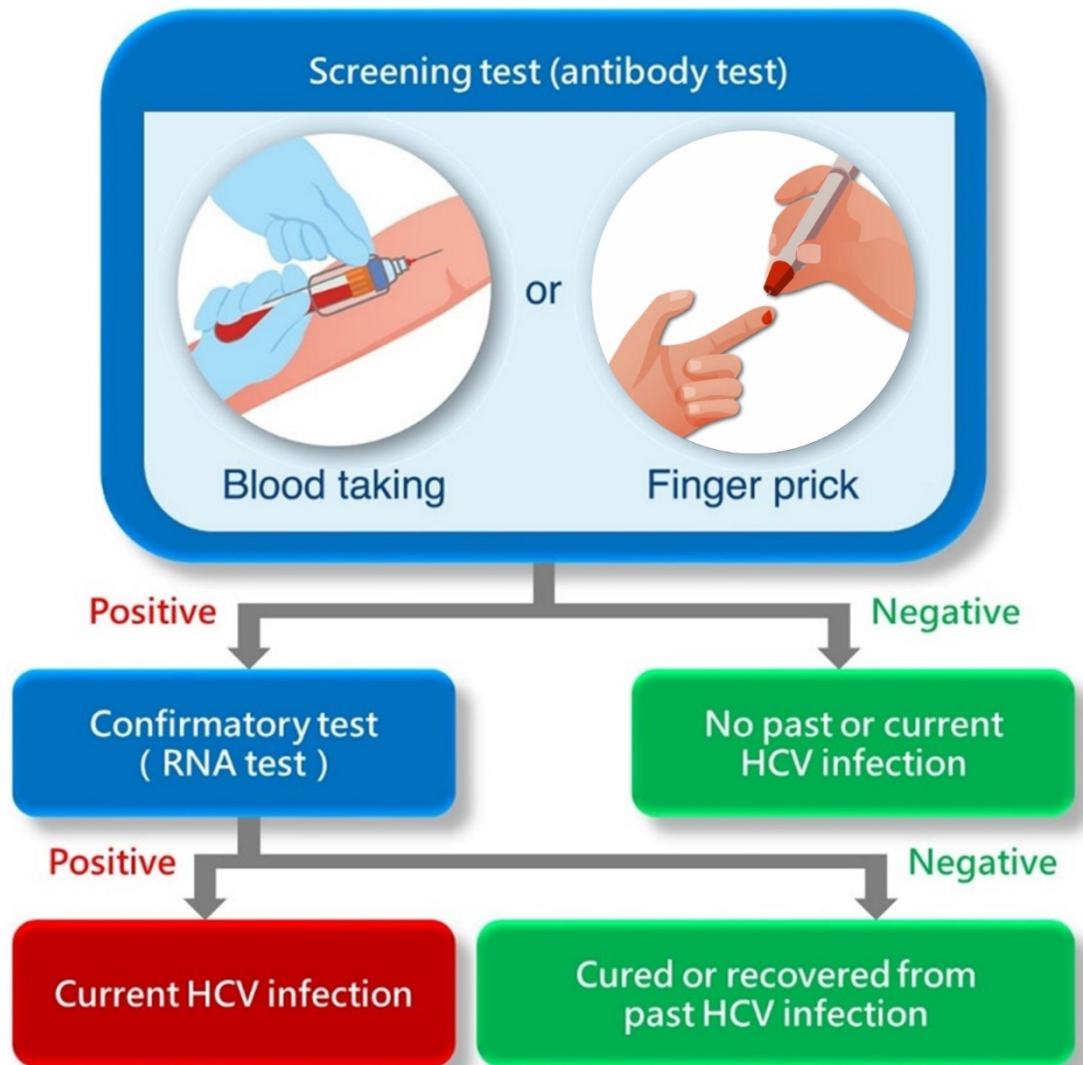
PWID are a hard-to-reach population because they may not be able to adhere to the highly structured secondary or tertiary healthcare settings in which HCV assessment and treatment are usually provided [29]. Recruiting PWID for health programme shall be considered in alternative institutions, such as methadone clinics and correctional facilities.

As set out in the Action Plan, a policy initiative to promote HCV testing in PWID, who are attending methadone clinics or under the custody of Correctional Services Department (CSD) has been established. Specific health education information about HCV infection tailored to PWID have been developed. Professional staff and other working serving PWID at methadone clinics, as well as CSD staff, have been engaged for promoting the importance of HCV infection. In addition, identification of testing options and algorithms for carrying out HCV testing for PWID is ongoing.

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A pilot programme involving selected methadone clinics has been conducted to assess the feasibility and acceptance of HCV testing among PWID and characterise the barriers to testing and linkage to care.

Figure 1. Flowchart for diagnosis of HCV infection



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Useful resources

Description of materials	Hyperlink	QR code	Cover
Pamphlet – What you need to know about hepatitis C	https://www.hepatitis.gov.hk/tc_chi/resources/files/What_you_need_to_know_about_hep_C.pdf		
Pamphlet – Getting tested for hepatitis C can save your life	https://www.hepatitis.gov.hk/tc_chi/resources/files/Pamphlet_Getting%20Tested%20for%20Hep%20C_WCAG.pdf		
Poster – Getting tested for hepatitis C can save your life	https://www.hepatitis.gov.hk/tc_chi/resources/files/Poster_Getting%20Tested%20for%20Hep%20C_WCAG_final.pdf		
Presentation slides – Hepatitis C virus infection	https://www.hepatitis.gov.hk/english/health_professionals/files/HCV_Intro_MC_doctors_web.pdf		
Video – Hepatitis C can cause liver cancer. Get tested and treated early	https://youtu.be/izlHUGAS6ao		
Video – Hong Kong Viral Hepatitis Action Plan 2020-2024	https://youtu.be/VaHs-DZWXEM		

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Test paper

Please submit the completed answer sheet within the validity period by email to hepatitis@dh.gov.hk.

CME/CPD: 0.5-1

CNE: 1

Validity Period: 31 March 2022 – 30 March 2023

College/ Programme	CME/ CPD Point	CME/CPD Category
Anaesthesiologists	1	PP-NA
Community Medicine	1	AP-SS
Dental Surgeons	1	OA-SS
Emergency Medicine	1	CME-PP
Family Physicians	N/A	N/A
Obstetricians and Gynaecologists	1	PP-PN
Ophthalmologists	1	CME-PP
Orthopaedic Surgeons	1	PP-B
Otorhinolaryngologists	0.5	PP-2.2
Paediatricians	1	D-AP
Pathologists	1	CME-SS
Physicians	1	AP-SS
Psychiatrists	1	SS-OL
Radiologists	N/A	N/A
Surgeons	1	CME-PP
MCHK CME Programme for Practising Doctors who are not taking CME Programme for Specialists	1	Passive (Accredited by DH)

Please contact respective authorities directly for CME/CPD accreditation if it is not listed above.

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1. Which of the following is **NOT** a correct description about the natural history of HCV infection?
 - A. Acute HCV infections are usually asymptomatic.
 - B. Most acute HCV infections do not cause life-threatening disease.
 - C. Development of chronic infection is common following acute HCV infection.
 - D. Spontaneous clearance of HCV within 12 months following acute infection can be achieved in more than 90% of people infected with HCV.
 - E. If left untreated, chronic HCV infection can lead to cirrhosis, hepatocellular carcinoma (HCC) and even death.

2. Which of the following is **NOT** a correct description about global epidemiology of HCV infection in PWID?
 - A. The World Health Organization (WHO) estimated that current injecting drug use (IDU) accounted for 23% of new HCV infections.
 - B. WHO estimated that 8% of current HCV infections were among PWID.
 - C. PWID infected with HCV are at increased risk of liver-related mortality but not all-cause mortality.
 - D. The latest systematic review gave an estimated number of anti-HCV-positive PWID at 8.2 million, corresponding to an anti-HCV prevalence at 52.3%.
 - E. Of all the deaths from cirrhosis and HCC due to HCV infection, 31% were attributable to a lifetime history of IDU.

3. Which of the following is **NOT** a correct description about local epidemiology of HCV infection in Hong Kong?
 - A. Past studies found an anti-HCV prevalence below 50% in PWID or ex-PWID.
 - B. Injection duration, current or recent injection, ever sharing injecting equipment and concomitant use of other drugs are associated with increased risk of HCV infection in PWID.
 - C. The prevalence of anti-HCV in the general population is about 0.5%.
 - D. IDU is an important route of HCV acquisition in Hong Kong.
 - E. The risk of transfusion-transmitted HCV infection in Hong Kong has decreased to a very low level since the institution of blood donor screening for HCV.

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4. Referring to the *Global health sector strategy on viral hepatitis, 2016 – 2021*, what are the relative reduction targets by 2030 for hepatitis C, as compared with the baseline number in 2015?
 - A. 80% reduction in incidence and 65% reduction in mortality
 - B. 80% reduction in incidence and 80% reduction in mortality
 - C. 90% reduction in incidence and 65% reduction in mortality
 - D. 90% reduction in incidence and 80% reduction in mortality
 - E. 95% reduction in incidence and 65% reduction in mortality

5. What are the absolute impact targets for hepatitis C incidence in 2030?
 - A. Annual HCV incidence of ≤ 10 per 100 000 persons and of ≤ 5 per 100 PWID
 - B. Annual HCV incidence of ≤ 10 per 100 000 persons and of ≤ 2 per 100 PWID
 - C. Annual HCV incidence of ≤ 5 per 100 000 persons and of ≤ 5 per 100 PWID
 - D. Annual HCV incidence of ≤ 5 per 100 000 persons and of ≤ 2 per 100 PWID
 - E. Annual HCV incidence of ≤ 1 per 100 000 persons and of ≤ 1 per 100 PWID

6. Which of the following is **NOT** a correct description about micro-elimination of HCV infection?
 - A. Micro-elimination refers to targeted elimination of HCV infection in well-defined populations.
 - B. The term “micro-elimination” emerges because HCV infection is a minor public health threat in most countries across all settings.
 - C. It is a strategy to achieve elimination incrementally through initiatives that eliminate hepatitis C for defined segments of the population, such as within settings, geographic areas, subpopulations and age cohorts
 - D. Targeting smaller and clearly delineated HCV risk groups allows faster and more efficient delivery of interventions.
 - E. The selection of targeted groups for micro-elimination initiatives should be based on the hepatitis C epidemiology and health context of different countries and subnational areas.

7. Which of the following does **NOT** belong to candidate populations for micro-elimination due to their higher burden of HCV infection?
 - A. Patients on haemodialysis
 - B. HIV/HCV co-infected people
 - C. Healthcare workers
 - D. People who inject drugs
 - E. Prisoners

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8. Which of the following is **NOT** the role of methadone treatment programme (MTP) in prevention and control of hepatitis C in Hong Kong?
- A. MTP is a harm reduction approach by providing a readily accessible, legal, medically safe and effective alternative to continued illicit self-administration of opiate drugs.
 - B. In Hong Kong, MTP is currently run by private healthcare organisations.
 - C. The objectives of MTP have been extended to reduce intravenous drug use and needle sharing and thereby prevent the spread of diseases like HIV/AIDS, viral hepatitis and other blood-borne diseases.
 - D. The network of methadone clinics affords the opportunity to engage PWID for health education and prevention of hepatitis C.
 - E. Some methadone clinics have been selected for conducting a pilot programme to assess the feasibility and acceptance of HCV testing among PWID and characterise the barriers to testing and linkage to care.
9. Which of the following is a correct description about the use of direct-acting antivirals (DAA)?
- A. DAA can only slow the progress of developing HCV-related complications and cannot cure most HCV infections.
 - B. Most DAA require intravenous administration.
 - C. Most patients taking DAA experience severe side effects, which make interruption of the HCV treatment common.
 - D. In Hong Kong, subsidised DAA treatment is limited to patients with advanced fibrosis or cirrhosis in the public health care settings.
 - E. DAA treatment has been expanded to cover all hepatitis C patients, irrespective of their stage of liver fibrosis, in the public sector in Hong Kong.
10. Which of the following is **NOT** one of the specific actions outlined in the Action Plan to promote HCV testing in PWID in Hong Kong?
- A. Establish a policy initiative to promote HCV testing in PWID, who are attending methadone clinics or under the custody of Correctional Services Department (CSD)
 - B. Provide specific health education information about HCV infection to PWID
 - C. Engage professional staff and other working serving PWID at methadone clinics, as well as CSD staff, for promoting the importance of HCV infection
 - D. Identify testing options and algorithms for carrying out HCV testing for PWID
 - E. Distribute HCV self-testing kits to PWID through the network of non-governmental organisation