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Short Communication

## Point-of-care hepatitis C reflex testing and treatment referral in methadone clinic settings in Hong Kong—a pilot study<sup>☆,☆☆</sup>

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### ABSTRACT

**Objectives:** People who inject drugs (PWID) constitute a population group with a high hepatitis C virus (HCV) burden. With the objectives of assessing the HCV prevalence in PWID and determining the proportion requiring treatment who could be linked to care, this study piloted onsite reflex HCV testing at low threshold methadone clinics, with prompt referral of HCV RNA-positive participants for treatment.

**Methods:** This was a prospective study on methadone clinic attendees in Hong Kong. Questionnaires were completed, finger-prick anti-HCV rapid testing was performed, and positive blood samples were collected for laboratory HCV RNA testing. The proportions of participants along the cascade of HCV care were calculated.

**Results:** In 2021–2022, after 14 evening screening sessions at three methadone clinics, 86 of 354 regular attendees (24%) were recruited. The anti-HCV prevalence was 63% (54/86, 95% confidence interval 52–73%), with 78% (42/54) testing positive for HCV RNA and 79% (33/42) successfully referred. Almost all (31/33) referred participants received direct-acting antiviral (DAA) treatment, 94% (29/31) with full treatment compliance; 55% (16/29) of these compliant participants achieved a sustained virological response, while the remainder had not received post-treatment testing.

**Conclusions:** The use of a simplified testing algorithm in the setting of substitution treatment services, incorporating reflex HCV testing, could be an effective strategy for contributing towards the micro-elimination of HCV in PWID.

### Introduction

Globally there are an estimated 15.6 million people who inject drugs (PWID), over half of whom are estimated to be positive for antibody against hepatitis C virus (anti-HCV) (Degenhardt et al., 2017), constituting a very high infection burden in the community. In 2016, the World Health Organization (WHO) called for the elimination of viral hepatitis (World Health Organization, 2016). As treatment plays an important role in hepatitis C virus (HCV) elimination, universal screening of PWID followed by the treatment of eligible patients is crucial. The global target of providing treatment to 80% of eligible persons with chronic HCV infection by 2030 remains a huge challenge (World Health Organiza-

tion, 2021). Micro-elimination, which involves tailoring interventions to discrete populations, including PWID, for pursuing elimination goals, is advocated as one of the key strategies to achieve the ultimate target (Lazarus et al., 2018; Messina et al., 2020). Effective direct-acting antivirals (DAA) hold the key to successful HCV control, but there are many barriers to scaling up diagnosis, linkage to care, and treatment for PWID (Day et al., 2019). In practice, opioid substitution treatment services targeting PWID provide convenient points of contact for the implementation of service initiatives for achieving HCV micro-elimination, but the capacity of these programs to incorporate HCV is often limited.

In Hong Kong, a low threshold methadone treatment program has been in operation for over half a century. The network of 19

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government methadone treatment clinics provides supervised daily methadone maintenance therapy exclusively for heroin users (Lee & Newman, 2017). Previous studies showed that over 80% of the heroin users in Hong Kong were infected with HCV (Wong et al., 2013). Despite a high daily caseload of around 4000 (Department of Health, 2020), methadone clinics are small operations without the health service capacity or staff to incorporate HCV testing and treatment within their portfolio. By reducing additional visits for the confirmation of HCV RNA test results, it is considered that a reflex HCV testing approach could promote linkage to HCV treatment. The initiation of a pilot project at three methadone clinics that provide onsite point-of-care reflex testing for HCV, with linkage to care at a neighboring hepatitis clinic, is reported here. Project objectives include estimating the HCV burden from the anti-HCV prevalence, and determining the proportion of HCV RNA-positive cases with linkage to care.

## Methods

Three evening methadone clinics serving attendees residing in the New Territories East Region of Hong Kong were selected as pilot sites. Four to five sessions, each lasting between 2 and 3 hours, were scheduled at each clinic to recruit consenting clinic attendees irrespective of their drug use history. Following completion of a questionnaire, a finger-prick test was performed, with the result known in 5 minutes: SD BIOLINE HCV point-of-care (POC) antibody testing. The finger-prick specimens of anti-HCV-positive subjects were collected and subsequently tested (i.e. reflex testing) in the laboratory with the Xpert HCV VL Fingerstick test in the ensuing days. Referral was made for HCV RNA-positive participants to attend a hepatitis specialist clinic at a teaching hospital in the same geographical region within 4 weeks. The process of recruitment, referral, and clinic attendance was assisted by volunteers from a community-based organization (CBO). DAA treatment was prescribed at the first consultation. The proportions of participants along the cascade of HCV care were calculated. Characteristics of the participants according to the study site were compared by Chi-square test using IBM SPSS Statistics software version 25 (IBM Corp., Armonk, NY, USA). Complete case analyses were performed for the handling of missing values.

## Results

Between May 2021 and January 2022, 14 screening sessions were organized at the three methadone clinics. Overall, 86 out of 354 regular attendees were recruited, all of whom were on methadone maintenance, half (49%) with a history of heroin use for over 30 years (Table 1). The majority (88%) were male, and the median age of the participants was 57 years (interquartile range 48–63 years). Most (95%) had continued using heroin in the preceding year, and 64% had ever practiced injection. There was variability between methadone clinics in the proportion of attendees with a needle-sharing history (ranging between 8% and 50%) and preferred HCV treatment location (Supplementary Material Table S1). Most of them preferred the current project's finger-prick sampling method (96%) and immediate provision of the result approach (94%). Thirty-seven out of 82 (45%) reported previous HCV testing and two out of 86 (2%) reported having received some form of treatment in the past.

The overall anti-HCV prevalence was 63% (54/86, 95% confidence interval (CI) 52–73%). A positive anti-HCV result was associated with using heroin in conjunction with other drugs (odds ratio (OR) 3.34, 95% CI 1.34–8.37), history of injection (OR 119, 95% CI 24.85–569.89), and long history of methadone maintenance (OR 1.04, 95% CI 1.003–1.08) (Table 1). Seventy-eight percent (42/54) of the anti-HCV-positive participants tested HCV RNA-positive, and all except nine were referred for treatment (four lost contact, five had self-arranged clinic attendance).

Ninety-four percent (31/33) of the participants referred to the specialist clinic attended their visit and were started on DAA treatment (24 on glecaprevir/pibrentasvir, seven on sofosbuvir/velpatasvir) within 4 weeks from testing. Full adherence was confirmed (29/31), except for two participants who did not attend the post-treatment evaluation. A sustained virological response at 12 weeks (SVR12) was documented in all 16 patients who attended the follow-up blood testing session, while 13 did not attend. An implementation cascade of the pilot test-and-treatment referral project at the methadone clinics is shown in Figure 1.

## Discussion

The coverage of methadone treatment among PWID in Hong Kong is high, at over 90% (Lee & Newman, 2017; Wong et al., 2013). With a low threshold program in place, the clinics do not have the capacity to offer an HCV testing and treatment service. In the absence of health service infrastructure support, this study highlights the importance of applying reflex POC testing as the anchor for enabling instantaneous screening followed by linkage to HCV care. This strategy allows an HCV diagnosis to be made without separate handling for RNA quantitation (Gale et al., 2011). The approach was well-accepted by clinic attendees receiving their daily dose of methadone in the clinics. Although HCV infection is associated with drug injection, testing was deliberately offered to every consenting participant to reduce stigmatization. The good linkage of HCV RNA-positive participants with DAA treatment and their achievement of SVR12 are in support of scaling up the piloted testing and treatment service. The treatment uptake of the study participants (74%, 31/42 HCV RNA-positive) was higher than that under the standard procedure (51%, 141/279 genotyped) (Hui et al., 2018). Having HCV testing performed at the person's familiar methadone clinic and providing treatment in a neighboring clinic were effective means of overcoming barriers for achieving HCV micro-elimination (Day et al., 2019).

This study carried certain inherent limitations. As it was organized as a research project, the HCV testing and information provision were done by study investigators with the support of volunteers from a CBO and clinic attendance in the neighborhood. The outcome would have been different in terms of coverage and acceptance of the service if they had been delivered by methadone clinic staff, who were better known to the attendees. Operationally, the duration and frequency of the screening sessions were restricted by the availability of clinic space, operating hours, and supporting facilities, which explains in part why only a quarter of the attending attendees were recruited. The small floor area size of the clinics and lack of medical service infrastructure did not allow onsite HCV RNA testing to be simultaneously performed in the same clinic session. Despite these shortcomings, the identification of methadone clinics as a setting for providing HCV screening and the support of CBO for reaching potential cases (Lai et al., 2021) form the basis for developing scaled-up programs to reach PWID in Hong Kong. Nevertheless, the selection of settings for onsite HCV screening may vary from place to place. The model in this pilot project may only be applicable to places with a similar epidemiology of heroin addiction and in the presence of high-coverage substitution treatment programs. The reflex testing and the strategy for linkage to care should be a useful reference in any locality, if and when DAA can be accessed by PWID without restrictions.

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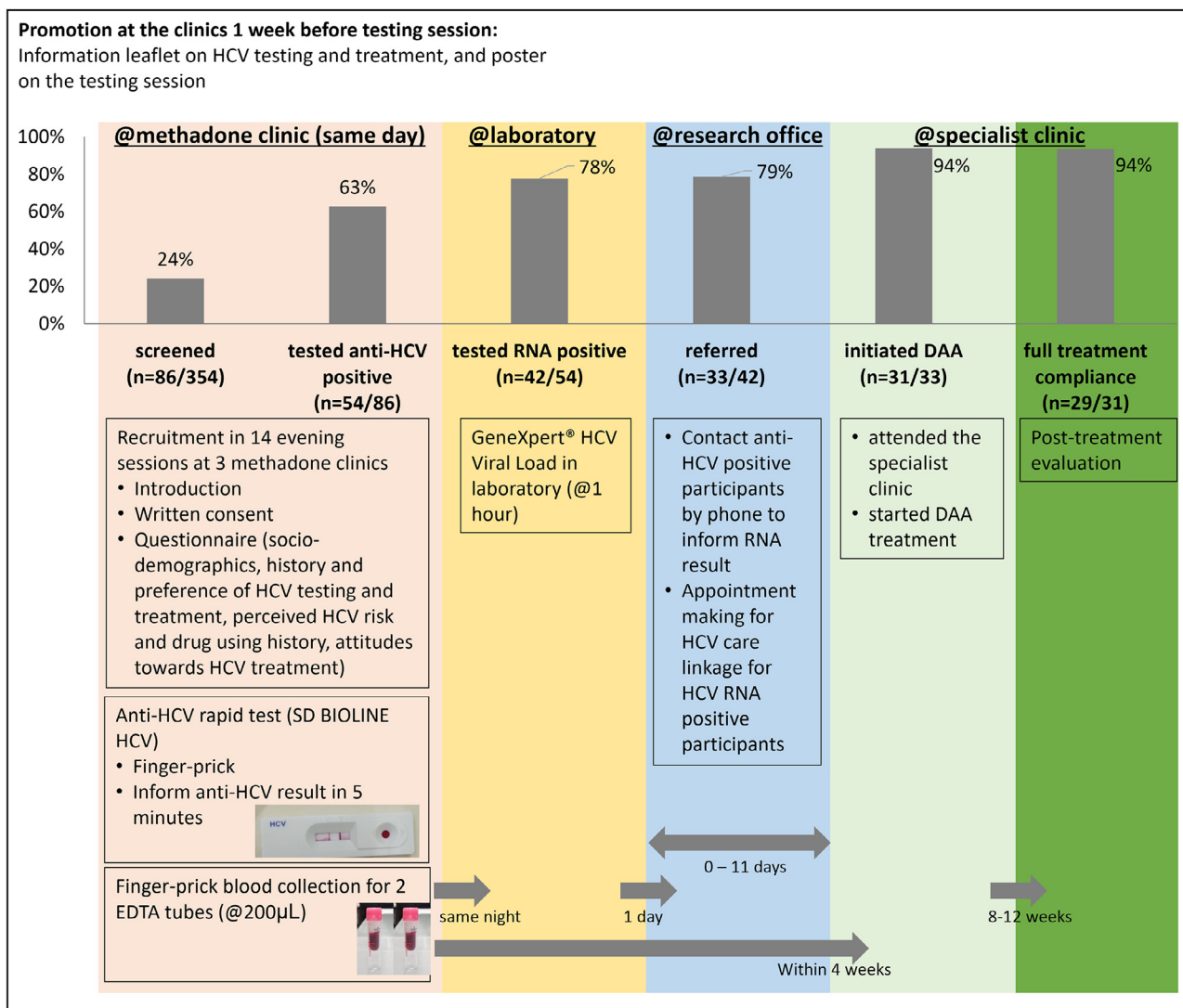
**Table 1**  
Comparison between anti-HCV-positive and anti-HCV-negative methadone clinic attendees (N = 86)

	Anti-HCV test result				Logistic regression	
	Negative (n = 32)		Positive (n = 54)		OR	95% CI
	n	%	n	%		
<b>Socio-demographics</b>						
<b>Sex</b>						
Female	4	40%	6	60%	Ref.	
Male	28	37%	48	63%	1.14	0.30–4.40
Age (years), median (IQR)	55.5	(47.5–64)	57	(48–62)	0.99	0.94–1.04
<b>Age<sup>a</sup></b>						
≤64 years	25	35%	46	65%	Ref.	
>64 years	7	47%	8	53%	0.62	0.20–1.91
<b>Ethnicity</b>						
Non-Chinese	2	100%	0	0%		
Chinese	30	36%	54	64%	/	
<b>Born in Hong Kong</b>						
No	7	33%	14	67%	Ref.	
Yes	25	38%	40	62%	0.8	0.28–2.25
<b>Local resident</b>						
No	1	50%	1	50%	Ref.	
Yes	31	37%	53	63%	1.71	0.1–28.31
<b>Education level</b>						
Primary or below	11	30%	26	70%	2.36	0.50–11.19
Junior secondary	17	41%	24	59%	1.41	0.31–6.45
Senior secondary	4	50%	4	50%	Ref.	
<b>Methadone history</b>						
Number of years of methadone use in Hong Kong, median (IQR) <sup>b</sup>	21	(10–32)	27	(21–37)	1.04*	1.003–1.08
<b>Methadone clinic</b>						
A	6	26%	17	74%	3.07	0.91–10.37
B	13	34%	25	66%	2.08	0.74–5.85
C	13	52%	12	48%	Ref.	
<b>History of drug use</b>						
Number of years since the first heroin use in Hong Kong, median (IQR) <sup>b</sup>	31	(18–39)	40	(25–42)	1.03	0.997–1.07
<b>&gt;30 years since the first use of heroin</b>						
No	20	45%	24	55%	Ref.	
Yes	12	29%	30	71%	2.08	0.85–5.1
<b>Ever drug use pattern</b>						
Heroin only	18	55%	15	45%	Ref.	
Heroin in conjunction with other drugs	14	26%	39	74%	3.34*	1.34–8.37
<b>Injection drug use</b>						
Never	28	90%	3	10%	Ref.	
Ever	4	7%	51	93%	119*	24.85–569.89
<b>Needle-sharing history</b>						
Never	4	11%	34	89%		
Ever	0	0%	14	100%	/	
<b>Perceived risk for HCV infection of the participant</b>						
0%	13	72%	5	28%	Ref.	
1–50%	14	61%	9	39%	1.67	0.44–6.31
50%	5	28%	13	72%	6.76*	1.57–29.07
51–99%	0	0%	8	100%	/	
100%	0	0%	14	100%	/	
Diagnosed	0	0%	5	100%	/	
<b>Awareness of HCV infection</b>						
<b>HCV infection is curable</b>						
No	21	44%	27	56%	Ref.	
Yes	11	29%	27	71%	1.91	0.77–4.71
<b>Awareness of existence of DAA regimen (oral medicines for 2–3 months)</b>						
Unaware	26	46%	30	54%	0.25*	0.06–0.96
Some idea	3	23%	10	77%	0.71	0.12–4.3
Clear yes	3	18%	14	82%	Ref.	

CI, confidence interval; DAA, direct-acting antiviral; HCV, hepatitis C virus; IQR, interquartile range; OR, odds ratio. \*P < 0.05.

<sup>a</sup> Age 64 years is a common cut-off for defining elderly in Hong Kong.

<sup>b</sup> Three missing.



**Figure 1.** Implementation of the cascade of HCV testing and referral for treatment, through project execution at pilot methadone clinic sites. The time interval between stages refers to the minimum and maximum range.

**Declarations**

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**Ethical approval:** Written informed consent was obtained from each participant in the pilot project. Ethical approval was obtained from the Joint Chinese University of Hong Kong—New Territories East Cluster Clinical Research Ethics Committee (CREC 2020.649) prior to the initiation of the study.

**Conflict of interest:** Grace Wong has served as a speaker for Abbvie, BMS, and Gilead Sciences, and on the advisory board for Gilead Sciences. Vincent Wong has served as a consultant or advisory board member for AbbVie, Boehringer Ingelheim, Echosens, Gilead Sciences, Intercept, Inventiva, Merck, Novo Nordisk, Pfizer, ProSciento, Sagimet Biosciences, and TARGET PharmaSolutions; and as a speaker for Abbott, AbbVie, Echosens, Gilead Sciences, and Novo Nordisk. He has received a research grant from Gilead Sciences, and is a co-founder of Illuminatio Medical Technology Limited.

**Supplementary materials**

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jregi.2022.08.007.

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