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ORIGINAL ARTICLE

Internet-guided HCV-RNA testing: A promising tool to achieve hepatitis C micro-elimination among men who have sex with men

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Abstract

In the Netherlands, hepatitis C virus (HCV) transmission occurs primarily in men who have sex with men (MSM). By early diagnosis and immediate treatment of acute HCV infections, HCV micro-elimination in MSM is within reach. In cooperation with the community affected, we developed an online HCV-RNA home-based self-sampling test service. This service combined online HCV self-risk assessment with the possibility to test anonymously for HCV-RNA. The service was available in the Netherlands from February 2018 till December 2020 and was promoted online on various dating sites and offline by community volunteers. Using website user data, test results and an online post-test user survey, we evaluated the service and user experiences. The website page with information about testing was visited by 3401 unique users, of whom 2250 used the HCV-risk assessment tool, 152 individuals purchased 194 HCV-RNA tests, and 104 tests were used, of which 101 gave a conclusive result. The target population of MSM at risk was successfully reached with 44.1% of users receiving the advice to test. The test service had a satisfactory uptake (6.8%, 152/2250), a very high HCV-RNA positivity rate (10.9%, 11/101) and was considered acceptable and easy to use by most MSM.

We demonstrate that an HCV-RNA home-based self-sampling test service is successful in diagnosing HCV infections among MSM. This service could be a valuable addition to existing sexual healthcare services as it may reach men who are otherwise not tested.

KEYWORDS

DBS, HCV, men who have sex with men, micro-elimination, self-sampled test

Abbreviations: DAA, direct-acting antivirals; DBS, dried blood spot; HCV, hepatitis C virus; MSM, men who have sex with men; PrEP, prophylaxis.

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1 | INTRODUCTION

Since 2000, hepatitis C virus (HCV) outbreaks among men who have sex with men (MSM) living with HIV have been reported globally.^{1,2} The Netherlands has had universal access to direct-acting antivirals (DAA) for HCV treatment in people living with HIV (PLWH) since November 2015. HCV incidence of HIV-infected men who have sex with men (MSM) in the Netherlands has sharply declined after DAA restrictions were lifted in 2015³ and HCV-viraemia among MSM living with HIV decreased from 3.9% in 2015 to 0.5% in 2019.⁴ These results suggest that the Netherlands is on track towards HCV micro-elimination in PLWH. Although the HCV reinfection rate also sharply declined from 41.4 per 1000 person-years in 2016 to 11.4 per 1000 person-years in 2019, it remains high.³ Additionally, HIV-negative MSM using pre-exposure prophylaxis (PrEP) to prevent HIV acquisition are also at substantial risk of HCV infection.⁵ A recent meta-analysis estimated a 123-fold higher HCV incidence in HIV-negative MSM using PrEP compared to HIV-negative MSM not using PrEP (pooled HCV incidence of 14.8 per 1000 person-years in HIV-negative MSM using PrEP).⁶ These findings illustrate that additional efforts are needed to achieve HCV elimination goals in MSM.

From the early 2000s, it has become clear that high-risk sexual and drug-related behaviours facilitate the spread of HCV among MSM.⁷ Early HCV diagnosis and immediate treatment and behavioural risk-reduction strategies may be effective to eliminate HCV in MSM.⁸ Client-initiated HIV self-testing services have been successful in increasing test uptake among MSM and trans people⁹ and may be a promising strategy to expand HCV testing and shorten time between infection and diagnosis.

HCV-RNA can be detected in the blood within 7–21 days after infection and is therefore the marker of choice for early diagnosis of HCV infection.¹⁰ In addition, HCV-RNA testing can be used to diagnose re-infections.

As part of the NoMoreC project, an innovative, multilevel intervention to reduce the HCV transmission among MSM in Amsterdam, we set up an anonymous Internet-guided HCV-RNA self-sampled test service for MSM at risk of HCV infection.¹¹ The C-test service assists users to assess their HCV-risk, gives personalized testing advice and information about different testing options. The service offers men the possibility to order a self-sampling HCV-RNA test kit, send their sample to the laboratory for testing and receive their test result anonymously online. Users who test HCV-RNA positive are linked to care to confirm their test result and start DAA treatment.

In this paper, we evaluate the use and outcomes of the test service and report user experiences.

2 | METHODS

2.1 | HCV testing service

The anonymous NoMoreC testing service was available to MSM in the Netherlands and used a validated home-based self-sampled dried blood spot (DBS) HCV-RNA test.¹² The testing service was

part of the NoMoreC project, a multilevel intervention developed and implemented at individual, community, healthcare professional, context, patient and network level. The co-creation process and development of the HCV testing service have been previously described in detail.¹¹ Briefly, we conducted focus group discussions with a group of MSM at risk of HCV to identify the needs regarding hepatitis C information and testing options. The community group recommended to use a test that detects the virus (instead of antibodies), also in men who have been infected in the past, and to offer a home-testing service. Based on this recommendation, an anonymous home-based HCV-RNA testing service guided by personal testing advice was proposed, which was received positively by the focus group participants. Subsequently, a website was developed (www.NoMoreC.nl) targeted at MSM at risk, providing information about hepatitis C, HCV transmission routes, risk reduction strategies, testing and treatment options, and partner notification. The website, available in Dutch and English, offered personalized online test advice, and the possibility to anonymously purchase an HCV-RNA test, called the C-test. Test advice was given, based on the validated HCV-MOSAIC score which consist of 6 self-reported risk factors (i.e. condomless receptive anal sex in previous 6 months, sharing of sex toys in previous 6 months, fisting without gloves in previous 6 months, injecting drugs in previous 12 months, sharing straws when snoring drugs in previous 12 months, and self-reported ulcerative STI (syphilis, genital herpes or lymphogranuloma venereum infection) in the previous 12 months).¹³ The HCV-MOSAIC score was developed to identify HIV-positive MSM at high risk for an acute HCV infection. The performance of the score among HIV-infected MSM in the development study showed a sensitivity of 78.0% and a specificity of 78.6% for acute HCV.¹³ The score was validated, using data from three studies, showing a sensitivity ranging from 73.1% to 100% and specificity from 56.2% to 65.2%.¹³

Users of the C-test service at risk of infection according to the HCV-MOSAIC risk score, and those who had been notified for HCV by a sexual partner, received the advice to get tested for HCV. Regardless of the test advice, users could subsequently purchase a test kit online (€25/test or €80/4 tests). Discount codes of 50%–100% could be used by those users who had seen the NoMoreC online promotional activities or flyers. Test kits were sent to the given address of the potential users (pseudonyms could be used), containing a DBS card with a unique number and barcode. Names or other identifying information were not printed on the DBS card and therefore could not be linked to the test result ensuring the anonymity of the service users. Users were informed by paper illustrations¹⁴ and an online instructional video¹⁵ on how to collect finger-prick blood samples. They were instructed to prick their finger with the lancets provided, place a drop of blood in each of the five circles on the DBS card, air dry the sample, place the DBS card in a grip seal bag with desiccant and subsequently in an envelope box. The envelope box needed to be placed in a postage-paid return envelope addressed to the laboratory of clinical virology of the Amsterdam University Medical Centers for HCV-RNA testing. All packaging materials were provided in the

test kit. Laboratory staff used the DBS card number and barcode for processing the test and authorizing the result. Users received an automated email notification when the result was entered in the system, which they could subsequently access with their personal login to the project website. Positive test results included a link to a referral letter, which users were advised to use for confirmation of their test result at the STI clinic, HIV treatment centre or GP practice. In addition, they were advised to prepare a contact list of all their sexual partners in the last 6 months to facilitate partner notification. Furthermore, a telephone number of a nurse practitioner was given to facilitate follow-up and give guidance to the user. For users who tested HCV-RNA negative, post-test information addressed risk-reduction strategies. In case of an inconclusive result, users were given the possibility to order a new test kit free of charge.

In February 2018, the NoMoreC website was launched and test kits could be purchased. The sale of test kits continued until November 2020. DBS samples, of the sold test kits, could be used until December 10, 2020. Online test results were accessible for the user until February 2021.

2.2 | HCV-RNA testing

Upon receipt of the DBS sample in the laboratory, two spots were cut out of the DBS card and eluted in L-6 buffer (500g GuSCN in 91.7 mL 0.2 M EDTA [pH 8.0], 10.12mL Triton X-100 and 416.7 mL 0.1 M Tris-HCl [pH 6.4]). The CAP/CTM assay (COBAS Ampliprep/COBAS TaqMan; Roche Diagnostics) was used for extraction, amplification and quantification of HCV-RNA on DBS eluates.

2.3 | Campaign design

From March 2018 till November 2020, the C-test service was promoted online on various gay dating applications and offline by the NoMoreC boy scouts, a team of volunteers recruited from the local community engaged in the project. Members of the team visited different gay events to promote the testing service. In addition, a promotional flyer was distributed by a leading pharmacy in Amsterdam (DC apotheek Valeriusplein) specialized in providing prescribed PrEP medication to men throughout the Netherlands. Discount codes of 50%–100% for a single test were distributed through the promotional activities to motivate men to purchase the C-test.

2.4 | Post-test survey

All users, who ordered a C-test kit, received a link to an online questionnaire by e-mail, 3 weeks after placing the order. No reminders to fill in the questionnaire were sent. The questionnaire, available in Dutch and English, contained questions about and reasons for

using the C-test service, acceptability of the C-test service, satisfaction with the service and NoMoreC website and possible problems with home sampling. Answer options included 5-point Likert scales, lists with pre-defined answers and open text fields (see Appendix 1 for the questionnaire and answer options). Participants gave their informed consent for scientific use of the questionnaire data by clicking the consent box prior to initiating the online questionnaire. The questionnaire responses were not linked to test results or users email addresses to ensure anonymity.

2.5 | Measures and outcomes

Website user data and test results were exported from the website, for the period 1 February 2018 to 31 December 2020. We collected data on

- Total number of visitors to the NoMoreC website;
- Total number of men who requested online test advice;
- Total number of men who received the advice to get tested, based on the HCV-MOSAIC score;
- Total number of men who received the advice that testing is not necessary, based on the HCV-MOSAIC score;
- Total number of men who received the advice to test based on a partner notification;
- Total number of men who ordered a C-test kit;
- Total number of men who used a discount code when ordering the kit;
- Total number of men who collected a DBS sample and returned it to the laboratory;
- Total number of positive and negative test results.

Descriptive analyses were used to assess the uptake (proportion of users who ordered a test kit after requesting test advice) return rate (proportion of ordered tests that were returned), positivity rate (proportion of test results that were HCV-RNA positive) of the test service and the characteristics of the users who ordered a test kit.

Furthermore, we assessed the level of agreement with statements regarding usability, acceptability and satisfaction of the service among all questionnaire respondents.

3 | RESULTS

3.1 | Uptake and results testing service

Between 1 February 2018 and 31 December 2020, the NoMoreC website was visited by 43,075 unique users (Figure 1). A third of the website users were returning visitors. The website page with information about testing was viewed 7127 times, of which 3,401 were unique page views (i.e. number of sessions in which the specified page was viewed at least once by a unique user). Of the users who visited the webpage about testing 66.2% (2250/3401) requested



FIGURE 1 Uptake and results of the Internet-guided HCV-RNA testing service from 1 February 2018 to 31 December 2020. DBS, dried blood spot; HCV, hepatitis C virus

online personalized test advice (Figure 1). A total of 194 HCV-RNA tests were ordered by 152 men, resulting in an overall uptake of the test service of 6.8% (152/2250). Discount codes were used by 73 men (48.0%) and 79 men (52.0%) paid the regular price of €25 for one test. Of the purchased tests, 53.6% (104/194) were returned to the laboratory, of which 97.1% (101/104) gave a conclusive result. Eleven out of 101 (10.9%) were HCV-RNA positive.

Of the website users requesting test advice, 44.1% (992/2250) received the advice to get tested, based on the risk score or having been notified by a sex partner, and 55.9% (1258/2250) received the advice that HCV testing was not necessary. Of the 992 website users who received the advice to test, 105 men (10.6%) ordered 141 test kits, of which 71 (50.4%) were returned to the laboratory. Seven out of 71 tests (9.9%) were HCV-RNA positive, 63/71 (88.7%) were negative and 1/71 (1.4%) could not be tested because the user had not sampled a sufficient amount of blood. Of the 1258 website users who received the advice that testing was not necessary, 47 (3.7%) ordered 53 test kits, of which 33 (62.3%) were returned to the laboratory. Four out of 33 tests (12.1%) were HCV-RNA positive, 27 (81.8%) negative and 2 (6.1%) were inconclusive because of a technical failure.

Among the users who received the advice to test, 16.2% (161/992) were notified by a sex partner, of whom 11 (6.8%) received the advice based on the partner notification only and 150 (93.2%) also based on the risk score. Nine per cent of the notified men (15/161) ordered one test. All 15 tests were returned to the laboratory of which two tests (13.3%) were HCV-RNA positive.

3.2 | Characteristics of survey participants

A total of 152 men who had ordered one or more tests received an email with a link to the online questionnaire between 22 February 2018 and 31 December 2020. The questionnaire was started by 86 participants and completed by 54, resulting in a response rate of 35.5% (54/152). All participants ($n = 54$) were MSM living in the Netherlands. The majority (44/54, 81.5%) were born in the Netherlands. The median age was 46 years (IQR 39–53). Two thirds reported they were HIV-negative (35/54, 64.8%) of whom 54.3% (19/35) were using PrEP. An HIV-positive status was reported by 15/54 men (27.8%), and 4/54 (7.4%) did not disclose their HIV status. Two thirds reported they had previously been tested for HCV (35/54, 64.8%). Previous testing took place at the STI clinic (17/35, 48.6%), hospital (12/35, 34.3%), GP practice (10/35, 28.6%) and NoMoreC testing service (3/35, 8.6%). Seven participants reported they had been tested at more than one location.

3.3 | Usability, acceptability and satisfaction with the test service

Most survey respondents (44/54 81.5%) had used the test kit, of whom 3/44 (5.6%) had reported a positive test result, 27/44 (61.4%) reported a negative test result, 11/44 (25.0%) did not disclose their

result and 3/44 (6.8%) had not yet received their test result. The three users who received a positive test result had their test result confirmed at their GP ($n = 1$) or STD clinic ($n = 2$) and were all linked to care. Ten respondents had not (yet) used the test kit for the following reasons: I am waiting until I have a reason to test (4/10, 40.0%), I have not had time to do the test yet (1/10, 10.0%), I was recently tested for HCV (1/10, 10.0%) and 4/10 (40.0%) respondents did not give a reason.

The majority of respondents were positive regarding C-test service usability, acceptability and satisfaction (Figure 2). Half of the respondents (27/54) reported that they found it easy to self-sample, 31.5% (17/54) found it difficult and 18.5% (10/54) did not answer the question. The main problem with sampling blood was to collect enough blood from the pricked finger to fill five circles on the sample card, which was reported by 16 of the 17 respondents who indicated self-sampling was difficult.

3.4 | Reasons for use of test service

Reasons for using the C-test service were reported by all questionnaire respondents ($n = 54$), and suggestions for improvement of the C-test were given by 8/54 respondents. The most common reasons for using the service were as follows: confirming their HCV-negative status, having concerns about being HCV-infected, saving time and the cheap price of the test (Table 1).

4 | DISCUSSION

To our knowledge, this is the first time an Internet-guided anonymous home-based self-sampling HCV-RNA test service, targeted at MSM at risk of acquiring HCV, was launched and evaluated. The service was developed and implemented in close conjunction with the community affected and combined a personalized test advice with the possibility to test anonymously for HCV.¹¹ We demonstrate that this service was successful in reaching its target population of MSM at risk of HCV as 44.1% of the users received the advice to test after

filling in a previously validated questionnaire,¹³ indicating that these men had been at risk of HCV in the past 6–12 months. Furthermore, we demonstrated that the service successfully diagnosed HCV infections with a positive test result in 10.9% of tests performed.

Considering that our C-test service was a user-initiated paid service offered in a country where STI testing is free of charge for MSM, the uptake of testing of 6.8% was satisfactory. Testing uptake following the advice to test might be higher as some men could have chosen to be tested elsewhere (e.g. at a STI clinic or HIV treatment centre). Interestingly, 3.7% of men who were advised that testing was not necessary, purchased a test kit. This suggests there is a need for men to know their current HCV status and that our service promoted pro-active testing. This is in line with our finding that 15% of the online questionnaire respondents reported as reason for purchasing the test its future use.

To the best of our knowledge, there are no other studies describing online user-initiated, home-sampled HCV-RNA testing services, and its uptake. Others have reported the uptake of home-sampled HIV and/or STI testing services for MSM. A Dutch pilot program offering home-sampling STI testing (chlamydia, gonorrhoea, hepatitis B and syphilis) to MSM living with HIV reported an uptake of 58% among their target group.¹⁶ The pilot was implemented in an HIV treatment centre, where healthcare providers offered free STI sampling kits to their clients during routine HIV care visits. The healthcare provider-initiated nature of the service as well as being free of charge may explain the higher uptake. A study from the UK reported an uptake of free home-based testing for HIV and/or hepatitis B and syphilis of only 1% among MSM.¹⁷ Similar to our C-test service, this service was user-initiated and offered online. The higher uptake among MSM in our study may be explained by the increased HCV risk awareness and testing needs of the group of MSM who were reached by our campaign and visited the NoMoreC website. A study describing a risk-based HCV antibody testing intervention targeted at people at risk in the general population in the Netherlands, reported an uptake of 28% among those who received the advice to test.¹⁸ This study also used an online questionnaire to assess risk and advice testing, but unlike our service participants received reminders by email or SMS and were referred to a laboratory for testing.

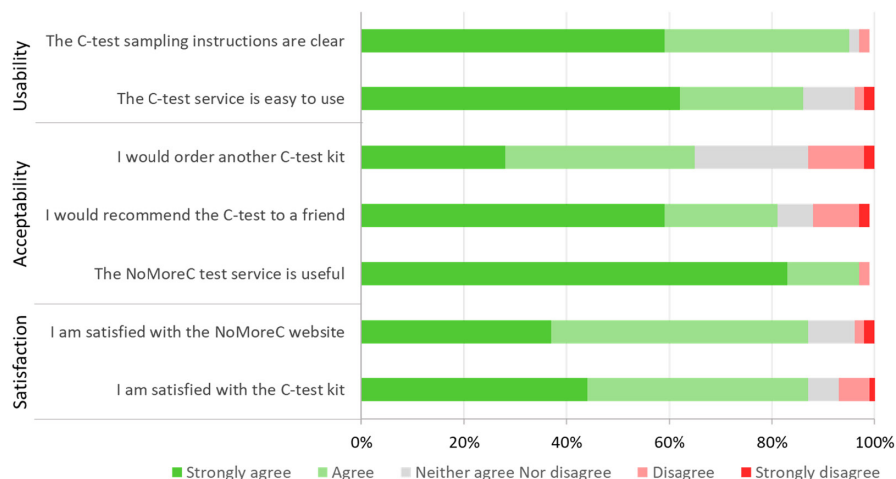


FIGURE 2 Level of agreement with statements about C-test usability, acceptability and satisfaction of 54 survey respondents who had ordered a C-test

TABLE 1 Reasons for use of the C-test service and suggestions for improvement reported by 54 participants who completed a survey 3 weeks after ordering a C-test kit

Reasons for using the C-test service
• I want to make sure I am not infected with HCV ($n = 33, 61.1\%$)
• I was worried I may be infected with HCV ($n = 20, 37.0\%$)
• It saves time ($n = 14, 25.9\%$)
• The test is cheap ($n = 14, 25.9\%$)
• I wanted to buy a test kit anonymously ($n = 10, 18.5\%$)
• I wanted to have a test-kit at home in case I need one in the future ($n = 8, 14.8\%$)
• I was curious about how the test service worked ($n = 7, 13.0\%$)
• I prefer not to talk about HCV-testing with my GP ($n = 6, 11.1\%$)
• I do not know any other way of getting tested for HCV ($n = 5, 9.3\%$)
• I bought the test kit for someone else ($n = 2, 3.7\%$)
• Because I take PrEP, I need to get tested for HCV ($n = 2, 3.7\%$)
• I was notified by a sex partner ($n = 1, 1.9\%$)
Suggestions for service improvement
• Improve the self-sampling instruction and give tips on blood collection ($n = 3, 37.5\%$)
• Improve instruction regarding packaging and posting of the blood sample ($n = 2, 25.0\%$)
• Integrate the C-test service with an existing online STI testing service ($n = 2, 25.0\%$)
• Include more than two lancets in the test kit ($n = 1, 12.5\%$)

More than one reason for C-test service use could be given. Suggestions for improvement were given by 8/54 participants.

This could indicate that sending reminders and offering the option to have blood sampled at a laboratory as an alternative to self-sampling at home, may increase uptake.

We found that our C-test service scored high on measures of usability, acceptability and satisfaction among its users. The main reasons for MSM to test for HCV through our service were to make sure they were not infected with HCV and being worried about an HCV infection. Time-saving, the relatively low price and the anonymous character of the service were also indicated as important. These factors are important in facilitating access to HCV testing. Some users stated that they did not know another way of getting tested for HCV, which shows that the C-test service has made testing more accessible. Hence, our service is a valuable addition to HCV testing at sexual health clinics, HIV treatment centres and GP practices.

Self-sampling of a good-quality DBS is crucial to the success of the service and dependent on clear sampling instructions. In our study, almost all users were able to sample an adequate DBS-sample and rated the instructions as clear or very clear. Yet, suggestions for improvement of the self-sampling instructions were given by the users. For future programs that will use a similar home-sampled testing approach, we recommend the production of easy-to-follow step-by-step instructions, including sampling, drying, packaging and posting instructions of the sample.

The overall rate of self-sampling and returning the home-based testing kits was 53.6% (104/194), which falls within the range of home sampling return rates for HIV and STI testing found in other studies (43.8%–84.5%).^{16,17,19,20} The return rate could potentially

have been higher if users had received reminders, as shown by studies that provided of self-sampling STI tests.¹⁶ Extending the evaluation period may also have resulted in a higher return rate as some users had indicated to have bought the kit for future use. These users may not have been at risk during the study period and hence had not returned their test.

Eleven new HCV infections were identified among the 104 MSM who returned their sample in the project period of 3 years (2018–2020). It is likely that these infections are among the 142 notified acute HCV infections among the general Dutch population, in 2018 and 2019,²¹ as all HCV-RNA-positive participants of the post-test survey reported they had followed the advice to confirm their test result at regular healthcare services.

The C-test service yielded an overall positivity rate of 10.9%. Among users who had received the advice to test based on the risk score or partner notification, the positivity rate was 9.9%. These rates are remarkably high, especially compared to a recent study at the STI clinic in Amsterdam that found a HCV-RNA positivity rate of 1.2% among MSM with HIV and transgender women who also were advised to test according to the HCV-MOSAIC score.²² Compared to free self-sampling HIV services in high-income countries for MSM, which have yielded positivity rates between 0.3% and 6.1%,²³ the positivity rate of our testing service is also high.

We recommend the continuation of an Internet-guided anonymous home-based HCV-RNA self-sampling testing service for MSM at risk of HCV, with targeted campaigns to encourage testing. Our service can facilitate early HCV diagnosis and prompt treatment, if the target population use the service to test shortly after having been at risk. MSM at increased risk of HCV are recommended to test every 3–6 months and to treat a recently acquired HCV infection immediately after diagnosis with DAAs.²⁴ Regular testing and high treatment success rates greatly reduce the HCV community reservoir and limit the pool for onward transmission.²⁵ A recent Dutch modelling study among HIV-positive MSM showed that early DAA treatment for acute HCV-infected men is a cost-saving prevention approach which indeed reduces the HCV incidence among this target population.²⁶ Assessing a reduction in time between infection and diagnosis when compared to standard care was outside the scope of our evaluation. However, this would be of interest to determine in the future as to be able to evaluate the impact of the testing intervention on the HCV epidemic.

This study also has limitations. First, we could not assess the reasons why men at risk did not order a test or if they decided to test elsewhere following a test advice. It would be insightful to understand their test behaviour and barriers to use of the C-test service, and to evaluate whether they can be lowered to increase uptake. Second, less than a third of the users of the test service completed the online questionnaire. Users who did respond may have been more positive or negative about the service than those who did not. Nevertheless, the questionnaire data were valuable to give an understanding of the user experiences. Third, we have limited knowledge about the reasons for not using the test kit

for those men who did buy a kit but did not return their home-sampled DBS.

In conclusion, the C-test service is a practical solution to improve access to HCV testing for MSM at risk and was considered acceptable and easy to use by most MSM. Our approach of offering online test advice combined with an anonymous Internet-guided HCV-RNA home-based self-sampling test service, in a country with unrestricted access to DAAs, contributes to reaching micro-elimination of hepatitis C among MSM. If the C-test service could be integrated in an existing Internet-guided STI testing platform, it could further increase access to testing and improve testing convenience for MSM at risk of HCV. Alternatively, the service could be offered as an additional testing service for those at risk of HCV infection next to routine HCV testing during PrEP and HIV care.

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CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

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