Eliminating hepatitis C: the importance of frequent testing of people who inject drugs in high prevalence settings

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Abstract

Modelling suggests that more frequent screening of people who inject drugs (PWID) and an improved care cascade are required to achieve the WHO hepatitis C virus (HCV) elimination target of an 80% reduction in incidence by 2030. We determined the testing frequencies (two-yearly, annually, six-monthly, three-monthly) and retention in care required among PWID to achieve the HCV incidence reduction target through treatment-as-prevention in low (25%), medium (50%) and high (75%) chronic HCV prevalence settings. Mathematical modelling of HCV transmission among PWID, capturing testing, treatment and other features of the care cascade were employed. In low prevalence settings, two-yearly antibody testing of PWID was estimated to reach the elimination target by 2027-2030 depending on retention in care, with annual testing reducing the time by up to three years. In medium prevalence settings, if close to 90% testing coverage were achieved then annual antibody testing of PWID would be sufficient. If testing coverage were lower (80%), six-monthly antibody testing with at least 70% retention in care or annual HCV RNA/cAg testing would...
be required. In high prevalence settings, even three-monthly HCV RNA/cAg testing of PWID alone was unable to achieve the incidence reduction target. Thus, for geographical areas or sub-populations with high prevalence, WHO incidence targets are unlikely to be met without three-monthly RNA testing accompanied by other prevention measures. Novel testing strategies, such as rapid point-of-care antibody testing or replacing antibody testing with RNA tests as a screening tool, can provide additional population-level impacts to compensate for imperfect follow-up or testing coverage.

INTRODUCTION

Prompt and accurate diagnosis of infection is a foundation of infectious disease control. This is because diagnosis is a necessary pathway to treatment, which can both directly reduce morbidity and mortality for individuals and also have population-level impacts through treatment-as-prevention (1). For hepatitis C virus (HCV), the recent availability of highly-effective direct-acting antiviral (DAA) treatments that are simple, have a duration of 8-12 weeks and minimal side-effects, have demonstrated rapid increases in uptake of DAA treatment to date (2). However, for population-level benefits to be maximised, additional efforts are needed to ensure diagnosis rates are high enough to generate sufficient treatment demand among key population groups.

Diagnosis of chronic HCV infection in most settings requires two steps. First, individuals undergo a test to detect HCV antibodies, which could be present due to acute, chronic or resolved infection. Individuals who are antibody positive are then required to undergo a follow-up polymerase chain reaction (PCR) test to detect HCV RNA, in order to distinguish current infections from previous infections. In most settings RNA tests are not currently used as an initial screening tool due to the higher associated costs (in the USA, Europe, Canada and Australia approximately US$70 compared to approximately US$14 for an antibody test (3-7)). A cheaper alternative in the future may be to use HCV core Antigen (HCVcAg) detection as a proxy for HCV RNA detection (8), with serum-based HCVcAg testing being shown to perform almost as well as PCR-based techniques (8, 9), but at a much cheaper price of approximately US$15-20 per test, similar to the cost of an antibody test. It is likely that HCVcAg tests will become more widely available throughout 2018.
The current constraint of two separate tests to obtain a complete diagnosis means that individuals are typically required to have at least three separate interactions with healthcare providers: 1) blood collection for antibody testing; if antibody positive 2) blood collection for HCV RNA/cAg test (as well as other clinical work up including fibrosis assessment); and 3) results of HCV RNA/cAg test and treatment commencement. This can be burdensome for individuals and has been associated with high rates of loss to follow-up, in particular among people who inject drugs (PWID), who have less engagement in traditional healthcare services than the general population and are a key risk group for HCV transmission and infection (10-12). This loss to follow-up among PWID has been identified as a major barrier to the success of treatment-as-prevention for HCV (13).

With the release of the World Health Organization (WHO) HCV elimination targets (14) and the increasing global availability of DAA treatments, many countries are developing national HCV strategies. For countries to achieve the WHO target of an 80% reduction in HCV incidence by 2030 through treatment-as-prevention, evidence-based testing strategies will be essential. Testing requirements for key risk populations will differ according to epidemic characteristics (such as initial HCV prevalence), health systems infrastructure, where the largest gaps are in the cascade of care, and should include guidelines for both the frequency of testing and types of tests used.

Mathematical models are useful tools that can generate scientific evidence to guide policies. In this paper we used a mathematical model to assess the likely impact of different test and treat scenarios on incidence reduction among PWID. For generalisability, we determine 1) the impact of two-yearly, annual, six-monthly and three-monthly testing, 2) alongside different rates of retention in care, for 3) settings where the chronic HCV prevalence among PWID is low (25%) (such as Czech Republic 25%, Tanzania 22%, and Uruguay 22% (12)); medium (50%) (such as Argentina 54%, Australia 55%, Iran 50%, the UK 51%, and Uzbekistan 52% (12)); or high (75%) (such as France 74%, Indonesia 77%, the USA 73%, and Vietnam 74% (12)).

METHODS

Model description
We used a dynamic compartmental model of HCV transmission among PWID as shown in Figure 1. The model population was divided into two groups: PWID and the remaining “general population”. People from either group could exit the model due to mortality, and the size of the combined population was held constant by the entry of uninfected individuals to the general population group. PWID in the model could move to the general population group due to cessation of injecting, and the total PWID population size was held constant by recruitment of additional members of the general population.

People in the model were classified as: susceptible (uninfected), infected but not diagnosed, infected and diagnosed antibody positive, infected and diagnosed HCV RNA/cAg positive, in treatment, or failed treatment. Susceptible individuals could become infected according to the current prevalence among PWID and a calibration constant, which was varied to achieve the desired equilibrium HCV prevalence.

People in the model were also classified as being covered by the healthcare system or not. Only the fraction of the population covered by the healthcare system could be tested, and testing was assumed to occur at an average (scenario dependent) frequency. A proportion of people who were diagnosed HCV-antibody-positive were modelled to have a follow-up HCV RNA/cAg test after an average duration 3 months, while the remaining proportion were lost to follow-up. These individuals were assumed to come into contact with the health system again (for their HCV RNA/cAg test) at their original testing rate. People who were diagnosed as HCV RNA/cAg positive were modelled to start treatment within 30 days. Those achieving SVR from treatment were moved back into the susceptible compartment where they had regular HCV RNA/cAg tests rather than regular antibody tests. Key model parameters are provided in Table 1 and further model details, including equations, calibration procedures and scenario implementations, are provided in the supplementary material.
In each scenario our primary outcome measure was the incidence reduction in 2030 relative to 2015 levels. From 2017, treatment was made available in the model with unrestricted access, the exception being that people in the model could only be treated if they had been diagnosed as HCV RNA/cAg positive.

In order to generalise across settings we ran scenarios with low (25%), medium (50%) and high (75%) HCV prevalence among PWID, and tested the impact of different testing frequencies and rates of retention in care. The particular scenarios considered are summarised in Table 2 and described below.

**HCV antibody testing policies and follow-up HCV RNA/cAg testing**

For settings with low, medium and high HCV prevalence among PWID, we used the model to estimate the incidence reduction in 2030 if antibody testing among PWID was (a) two-yearly, (b) annually, (c) six-monthly, or (d) three-monthly. The scenarios (a)–(d) were run with follow-up rates of HCV RNA/cAg testing among PWID (defined as an HCV RNA/cAg test within 3 months) ranging between 50% and 100%. Increases in testing frequencies and retention in care were scaled up over a five-year period.

A base level of 80% HCV antibody testing coverage among PWID was assumed (representing what might be achievable if testing were delivered through OST and NSP sites (23), and comparable to the percentage of PWID who have been tested for HCV in the USA (74% (24)), England (86% (25)), Scotland (92% (25)) and Australia (93% (26))). However, alternate scenarios were also run with 70% and 90% testing coverage.

**Replacing HCV antibody testing with HCV RNA/cAg testing**

For the settings with low, medium and high HCV prevalence among PWID, we used the model to estimate the incidence reduction in 2030 if the time lag between HCV antibody testing and HCV RNA/cAg testing was eliminated. This could occur by using HCV RNA/cAg testing as a screening tool without any preliminary HCV antibody testing (assuming HCVcAg testing to be equally as effective as PCR-based RNA testing, which initial trials indicate is likely to be the case for serum-based versions.
(8, 9)), or using rapid HCV antibody testing followed by same day HCV RNA/cAg testing in antibody positive patients. This scenario (HCV RNA/cAg testing only or zero time between HCV antibody and RNA/cAg tests) was run for testing occurring (a) two-yearly, (b) annually, (c) six-monthly, or (d) three-monthly. This scenario also assumed a base level of 80% testing coverage among PWID, as well as alternate scenarios with 70% and 90% testing coverage.

*Sensitivity analysis*

The theoretical PWID populations that we modelled are deliberately general and represent an “average” PWID population in a developed country. This was done in order to make the outcomes relevant at an international level to inform global guidelines. However, some of the underlying PWID parameters used in the model (Table 1) are necessarily taken from specific settings. To better understand the applicability of our results to individual countries it is important to know if or how our outcomes would change for different parametrizations. Therefore we re-ran all scenarios with a series of alternate assumptions aiming to reflect the extent of between-setting variations: an average length of injective career of 8.5 years instead of 17 years; a mortality rate among PWID of 4.70 or 1.18 instead of 2.35 per 100 person-years; treatment effectiveness of 90% rather than 95% to reflect possible lower adherence or uptake following diagnosis; and an average time from complete diagnosis to treatment commencement of 60 days rather than 30 days.

Our main outcome measure was incidence reduction in 2030; however projections of prevalence and incidence among PWID over time are provided in the supplementary material (Figures S2-S4) to show the epidemic trajectories of different testing frequency, testing coverage and retention in care scenarios.

**RESULTS**

**Low prevalence setting**
In a setting with low chronic HCV prevalence among PWID, two-yearly antibody testing among PWID was able to reach the incidence reduction target by 2030 if at least 80% testing coverage could be achieved (Figure 2A, Figure 2B and Table 3). However if testing frequency was increased to six-monthly, this was achieved by 2024 (Table 3).

**Medium prevalence setting**

In a setting with medium chronic HCV prevalence among PWID, even with 90% testing coverage and 100% retention in care, two-yearly antibody testing among PWID was not sufficient to achieve the incidence reduction target (Table 4). With 90% testing coverage, annual antibody testing of PWID could reach the incidence reduction target between 2027 and 2029 depending on retention in care (Table 4). If testing coverage was more realistically 80% of PWID, then annual antibody testing was no longer able to reach the target and six monthly testing was required, along with at least 60% retention of antibody positive patients in care (Table 4 and Figure 2C).

For settings where high-coverage of annual antibody testing or six-monthly antibody testing with close to 100% follow-up are seen as impractical, it may become realistic to replace HCV antibody testing with HCV RNA/cAg testing as a screening tool. This removes an opportunity for loss to follow-up. When this was implemented in the model an 80% reduction in incidence was achieved by 2030 with annual HCV RNA/cAg testing of PWID (Table 4 and Figure 2D) and 80% testing coverage (Table 4).
High prevalence setting

In a setting with high (75%) prevalence among PWID, both three-monthly HCV antibody testing with 100% retention in care and three-monthly HCV RNA/cAg testing of PWID with 90% coverage were insufficient to reach the incidence reduction target when used without prevention activities (Figure 2E and Figure 2F).

Sensitivity analysis

When the analyses were re-run with alternate PWID parameter assumptions, qualitatively similar results were found due to modest impacts on the longer-term (2030) incidence reduction relevant for the HCV elimination target. In low prevalence settings, two-yearly antibody testing of PWID with at least 80% coverage was required to reach target in all parameter scenarios except when treatment was only 90% effective, in which case annual antibody testing was required. In medium prevalence settings, if close to 90% testing coverage could be achieved then annual antibody testing of PWID was sufficient in all parameter scenarios except where treatment was only 90% effective, in which case the targets were not reached even with three-monthly testing. In high prevalence settings, testing alone was unable to reach the incidence reduction target in all parameter scenarios. Figure S5 shows the results for the high prevalence setting (which had the greatest variation) using 80% testing coverage.

DISCUSSION

For low, medium and high prevalence epidemic settings we used a mathematical model to determine the testing frequencies and retention in care required among PWID, in addition to universally available DAA treatments for HCV, to reach the WHO target of an 80% reduction in incidence by 2030. The results demonstrate that the testing strategies required to achieve HCV elimination vary markedly by initial chronic HCV prevalence, highlighting the extent to which public health strategies need to be tailored to the country context. Substantially lower testing frequencies are required in those contexts with low initial chronic HCV prevalence among PWID, compared to settings with higher initial prevalence. For much of the world where PWID drive the HCV epidemic and 50% or more are chronically infected, testing frequency needs to become a critical component of elimination strategies in order to meet 2030 targets.
Our model suggests that in low prevalence settings, if treatments were made universally available then two-yearly antibody testing of PWID would likely be sufficient if supported by at least 50% linkage to care. More frequent testing could reduce the time to reach the elimination target from 2030 with two-yearly testing to 2025 with six-monthly testing. In medium prevalence settings, annual antibody testing of PWID would be sufficient if high testing coverage could be achieved (supported by at least 50% linkage to care), otherwise six-monthly antibody testing of PWID with high retention in care would be required to compensate. In high prevalence settings, even three-monthly HCV RNA/cAg testing of PWID with 100% linkage to care was not able to achieve the incidence reduction target. In these settings additional primary prevention measures such as increases in needle and syringe programs and opioid substitution therapy coverage among PWID will be required to achieve the greatest reduction in incidence. These harm reduction programs have been shown to reduce the risk of HCV infection among PWID by more than 50% (27), and can significantly increase the impact of treatment (28).

In medium and high prevalence settings, consideration also needs to be given to the feasibility of high-frequency testing of PWID. For example, in Australia, a setting with large public health emphasis on HIV testing and the availability of a range of novel testing methods, less than half of high-risk men who have sex with men have an HIV test at the recommended 6-monthly frequency (29). For PWID, a population who are far less engaged in healthcare services (30-32), this suggests that alternate approaches to high-frequency antibody testing with follow-up HCV RNA/cAg testing will be needed.

One alternate approach to HCV diagnosis may be to use rapid point-of-care (POC) antibody tests as a screening tool for PWID. This would effectively be an “HCV RNA/cAg screening”, as it would eliminate the need for a return appointment for antibody-positive patients. Since 2016, POC tests have become available that can detect HCV antibodies within 30 minutes from patient saliva swabs (33). These tests are currently being trialled in community settings with initial findings suggesting that they are highly effective at reducing patient loss to follow-up between HCV antibody and HCV RNA/cAg testing stages (34). If this strategy could produce close to 100% follow-up, then in medium prevalence settings annual testing may be sufficient to reach the incidence reduction target.
A second approach to improve HCV diagnosis is to simply replace antibody tests with RNA tests as a screening tool among PWID; however, cost is a major barrier to this approach, with RNA tests costing nearly five times as much as antibody tests (3-7). As the number of cured PWID increases, so too will the number of antibody positive but HCV RNA/cAg negative individuals who require HCV RNA/cAg testing as a screening tool. Therefore, the continued development of affordable HCV rapid diagnostics that can distinguish past and current infection will be a critical ongoing issue. There are already novel RNA tests becoming available that mean the costs are decreasing. For example, Xpert® HCV Viral Load assay (Cepheid, CA, USA) was launched in 2015 as a POC diagnostic test for HCV RNA, using either venepuncture-collected or finger-stick capillary whole-blood samples to detect the presence of HCV RNA within 90 minutes (35-37). The costs of these tests are estimated to be approximately US$50 per test, cheaper than the current RNA tests (approximately US$70 for standard PCR tests (3-7)). When we modelled the replacement of antibody testing with HCV RNA/cAg testing as a screening tool for HCV infection among PWID, we found additional incidence reduction could be achieved. This was due to the removal of loss to follow-up between HCV antibody and HCV RNA/cAg tests, and for patients retained in care the removal of a time period when infected individuals can continue to transmit infection. Previous modelling suggests that this additional incidence reduction is likely to reduce future treatment and healthcare costs enough to outweigh the additional testing costs; (13) however such a strategy would still require significant upfront investment. Our model suggests that in medium prevalence settings, annual HCV RNA/cAg testing would be sufficient to reach the WHO incidence reduction target, even with imperfect testing coverage, such as what might be provided through needle and syringe programs and opioid substitution therapy services.

A third and cheaper approach to improve HCV diagnosis may be to use HCVcAg as an alternate screening tool to detect active HCV infection (8). HCVcAg test are estimated to cost US$15-20 per test, and can be performed using either serum or dry blood spot techniques. Serum-based HCVcAg testing performs almost equally as well as PRC-based techniques (8, 9), but it is not currently available as a POC test meaning that coverage is limited by the reliance on appropriate sample storage. Dry blood spot HCVcAg testing offers much greater coverage potential, but has been found to be a less sensitive than serum-based HCVcAg or standard PCR-based tests (9). As HCVcAg tests become available, further work is required to assess the role that they can play within the elimination strategies of individual countries, especially those with limited resources and healthcare infrastructure. A key question is whether the additional coverage and subsequent treatment delivery...
associated with dry blood spot HCVcAg testing, particularly in rural areas, outweighs the cost of the missed opportunities resulting from the lower test sensitivity. In our model this would produce similar results to scenarios with slightly lower testing coverage.

In this study we assumed that once diagnosed HCV RNA/cAg positive, individuals would commence treatment within 30 days. There are a number of reasons, including cost, additional clinical guidelines (e.g. requiring genotyping or assessment for other blood borne viruses), lack of motivation, feelings of stigmatisation (real or perceived) that may make this assumption optimistic, and in practice many may individuals may either delay treatment commencement or elect not to be treated at all. We tested these scenarios in the sensitivity analysis and found that doubling the average time to start treatment to 60 days had minimal impact, but if many PWID elected not to start treatment at all following diagnosis this could have significant implications for achieving elimination. When we changed the treatment success rate from 95% to 90%, which would also reflect a scenario of 5-10% of PWID electing not to be treated, the incidence reduction target could no longer be reached in a medium prevalence setting, even with three-monthly testing. This highlights some of the challenges associated with HCV elimination.

Total costs and cost-effectiveness are major drivers of policy decisions and should feature in a countries decision to adopt particular testing guidelines. In high-burden settings or in settings with large PWID populations or high diagnostic costs, it might be the case that these levels of HCV testing are unaffordable. Where limited resources are available, trade-offs between investing more in the provision of HCV treatment compared to increasing testing should be evaluated using cost-effectiveness analysis. This is an important area for future work; country-specific inputs should be assessed to determine how close they countries come to the elimination targets for a given available budget.

It is important to note that while the average HCV prevalence among PWID within a country is a key indicator for the development of general guidelines for HCV elimination strategies, the most appropriate testing frequency may vary between individual PWID within the same country. For example, it is likely that some individuals may require more frequent testing as a result of particularly high-risk behaviour or high-risk circumstances (e.g. incarceration). A limitation to this study is the lack of epidemiological data to inform reinfection rates following treatment in the DAA
era—in particular if and how rates of reinfection differ from initial infection, and risk factors driving these differences. This should be considered in future epidemiological studies. The geographical distribution of HCV is also heterogeneous in many countries, meaning that although a country may be considered low prevalence overall, some geographic areas may fall into the high prevalence category. Therefore, appropriate guidelines should be based on high-resolution data where available.

A limitation of this study is that our approach to generalise the model to a range of settings was to vary the HCV prevalence among the key population of PWID. There are other key parameters describing PWID populations that were not tailored to specific settings; however we ran sensitivity analyses on these parameters and found that they did not qualitatively change our results. This means that when applied to specific settings, variations in the PWID parameters such as length of injecting career are unlikely to change the outcome. We also assumed that prior to treatment scale-up, transmission and prevalence of HCV among PWID was relatively stable. This type of epidemic is common of many developed countries but may limit the applicability of these results to countries with more generalised epidemics, or epidemics with high levels of transmission occurring within the healthcare system. The aim of this study was to provide evidence to inform HCV testing guidelines rather than broader elimination strategies, and therefore the model did not include increases in the coverage of primary prevention programs such as needle and syringe programs and opioid substitution therapy. These programs have been found to be effective at reducing incidence elsewhere (27, 28), and their expansion would increase the impact of each testing and treatment scenario and bring forward the year that the incidence reduction target was reached.

In conclusion, novel testing strategies for PWID will be required to reach the WHO incidence reduction target in medium and high prevalence settings. In medium prevalence settings, annual testing to establish HCV RNA/cAg status will be required. Advancements in testing make this possible by either using rapid POC antibody testing to increase retention in care between antibody and HCV RNA/cAg testing stages, or replacing antibody testing with the use of HCV RNA/cAg tests as a screening tool. For areas or populations with high prevalence, even three-monthly HCV RNA/cAg testing needs to be combined with other prevention measures to achieve the WHO incidence reduction targets.
AUTHOR CONTRIBUTIONS

NS performed the modelling and drafted the manuscript. NS and MH conceived the study. All authors provided model interpretation and contributed to the manuscript.

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DECLARATION OF INTERESTS

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REFERENCES


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### Tables

Table 1: Summary of key model parameters

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<thead>
<tr>
<th>PWID parameters</th>
<th></th>
</tr>
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<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>PWID population size</td>
<td>—</td>
<td>Outcomes are based on relative reductions, making the population size arbitrary / scalable in the model.</td>
</tr>
<tr>
<td>Average duration of injecting career</td>
<td>17 years</td>
<td>(15) Tested in sensitivity analysis.</td>
</tr>
<tr>
<td>PWID mortality rate</td>
<td>2.35 per 100 person-years</td>
<td>(16) Tested in sensitivity analysis.</td>
</tr>
<tr>
<td>HCV parameters</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic HCV prevalence in 2016</td>
<td>25%/50%/75%</td>
<td>Three settings tested.</td>
</tr>
<tr>
<td>Probability of spontaneous clearance</td>
<td>26%</td>
<td>(17)</td>
</tr>
<tr>
<td>Infection / reinfection risk</td>
<td>Calibrated</td>
<td>The force of infection was assumed proportional to the time-varying prevalence in the model multiplied by a constant. This constant was calibrated to produce the desired chronic HCV prevalence. Reinfection was assumed to occur at the same rate as initial infection. Further details are in the supplementary material.</td>
</tr>
<tr>
<td>Treatment effectiveness</td>
<td>95%</td>
<td>(18-21)</td>
</tr>
<tr>
<td>Treatment duration</td>
<td>12 weeks</td>
<td>(18-20, 22)</td>
</tr>
<tr>
<td>Proportion engaged in care / testing for HCV</td>
<td>Varied in scenarios</td>
<td></td>
</tr>
<tr>
<td>Rates of care cascade progression</td>
<td>Varied in scenarios</td>
<td></td>
</tr>
<tr>
<td>Average time from RNA/cAg diagnosis to treatment initiation</td>
<td>30 days</td>
<td>This is an optimistic assumption and tested in the sensitivity analysis.</td>
</tr>
<tr>
<td>Table 2: Scenarios considered for the HCV antibody + RNA/cAg testing protocols and HCV RNA/cAg-only testing protocols.</td>
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<td></td>
</tr>
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<table>
<thead>
<tr>
<th>HCV prevalence among PWID</th>
<th>25%, 50%, 75%</th>
<th>25%, 50%, 75%</th>
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</thead>
<tbody>
<tr>
<td>Testing frequency</td>
<td>3, 6, 12, 24 monthly</td>
<td>3, 6, 12, 24 monthly</td>
</tr>
</tbody>
</table>
Table 3: Year elimination target reached with various test and treat scenarios, low prevalence setting (25% chronic HCV prevalence among PWID). Dashes indicate scenarios where an 80% reduction in incidence was not achieved by 2030.

<table>
<thead>
<tr>
<th>Testing coverage</th>
<th>Two-yearly</th>
<th>Annual</th>
<th>Six-monthly</th>
<th>Three-monthly</th>
</tr>
</thead>
<tbody>
<tr>
<td>70%, 80%, 90%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percentage followed-up for further testing within 3 months</td>
<td>50–100%</td>
<td>N/A</td>
<td></td>
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</tr>
</tbody>
</table>
Table 4: Year elimination target reached with various test and treat scenarios, medium prevalence setting (50% prevalence among PWID). Dashes indicate scenarios where an 80% reduction in incidence was not achieved by 2030.

<table>
<thead>
<tr>
<th>Testing frequencies</th>
<th>Two-yearly</th>
<th>Annual</th>
<th>Six-monthly</th>
<th>Three-monthly</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>70% 80% 90%</td>
<td>70% 80% 90%</td>
<td>70% 80% 90%</td>
<td>70% 80% 90%</td>
</tr>
<tr>
<td>Antibody testing with 50% follow-up RNA/cAg testing</td>
<td>-- -- --</td>
<td>-- -- 2029</td>
<td>-- -- 2026</td>
<td>-- 2029 2024</td>
</tr>
<tr>
<td>Antibody testing with 60% follow-up RNA/cAg testing</td>
<td>-- -- --</td>
<td>-- -- 2028</td>
<td>-- 2030 2026</td>
<td>-- 2029 2024</td>
</tr>
<tr>
<td>Antibody testing with 70% follow-up RNA/cAg testing</td>
<td>-- -- --</td>
<td>-- -- 2028</td>
<td>-- 2030 2025</td>
<td>-- 2029 2024</td>
</tr>
<tr>
<td>Antibody testing with 80% follow-up RNA/cAg testing</td>
<td>-- -- --</td>
<td>-- -- 2028</td>
<td>-- 2030 2025</td>
<td>-- 2029 2024</td>
</tr>
<tr>
<td>Antibody testing with 90% follow-up RNA/cAg testing</td>
<td>-- -- --</td>
<td>-- -- 2027</td>
<td>-- 2030 2025</td>
<td>-- 2029 2024</td>
</tr>
<tr>
<td>Antibody testing with 100% follow-up RNA/cAg testing</td>
<td>-- -- --</td>
<td>-- -- 2027</td>
<td>-- 2030 2025</td>
<td>-- 2029 2024</td>
</tr>
<tr>
<td>RNA/cAg testing only</td>
<td>-- -- --</td>
<td>-- 2030 2027</td>
<td>-- 2029 2024</td>
<td>-- 2028 2023</td>
</tr>
</tbody>
</table>

Figure legends

Figure 1: Model schematic

Figure 2: 2030 incidence reductions with various test and treat scenarios. Left column: for settings with 25% (A), 50% (C) and 75% (E) HCV prevalence among PWID, projected incidence reduction with
two-yearly, annually, six-monthly or three-monthly HCV antibody testing among PWID, in combination with different levels of follow-up HCV RNA/cAg testing. Coverage of antibody testing is assumed to be 80% of PWID. Right column: for settings with 25% (B), 50% (D) and 75% (F) HCV prevalence among PWID, projected incidence reduction when HCV antibody testing was replaced with HCV RNA/cAg testing among PWID.
Projected 2030 incidence reduction among PWID for test and treat scenarios

(A) 25% prevalence: Ab + follow-up RNA/cAg testing
- 50% RNA/cAg tested within 3 months
- 60%
- 70%
- 80%
- 90%
- 100% RNA/cAg tested within 3 months

(B) 25% prevalence: RNA/cAg testing only
- 70% testing coverage
- 80% testing coverage
- 90% testing coverage

(C) 50% prevalence: Ab + follow-up RNA/cAg testing

(D) 50% prevalence: RNA/cAg testing only

(E) 75% prevalence: Ab + follow-up RNA/cAg testing

(F) 75% prevalence: RNA/cAg testing only

2-yearly testing, Ab testing, 6-monthly 3-monthly testing
- 60% cov.
- 80% cov.

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