NICE advice

The OraQuick HCV point-of-care test for rapid detection of hepatitis C virus antibodies

Medtech innovation briefing
Published: 2 March 2015

www.nice.org.uk/guidance/mib24

Summary

The OraQuick HCV test detects antibodies against hepatitis C virus and can be used on oral fluid, fingerstick blood, venous blood, plasma or serum, giving results in 20 to 40 minutes. Eleven published studies showed that the OraQuick HCV has very high sensitivity and specificity. The cost per test is £12 to £15.

Product summary and likely place in therapy

- The OraQuick HCV is a rapid, point-of-care diagnostic test to identify anti-hepatitis C virus (HCV) antibodies. It can be used with oral fluid, fingerstick blood, venous blood, plasma or serum. It provides a result after 20 to 40 minutes and is quicker than testing venous blood samples or dried blood spot samples for anti-HCV antibodies in a laboratory.

- The OraQuick HCV is intended for use in the community, in GP practices or in mobile clinics targeted towards people at risk of hepatitis C (HCV).
- In the case of a positive test result with either the OraQuick HCV or conventional testing, further investigation is needed to determine whether active virus is present and whether the person needs treatment.

Effectiveness and safety

- Eleven studies were included in this briefing, 9 of which reported diagnostic performance data. Of these studies, 7 used oral fluid samples for OraQuick HCV testing and 9 used blood (fingerstick or venous blood) or blood-fraction samples (plasma, serum). Five studies used the OraQuick HCV in a community or mobile clinic setting and 2 studies looked at cross-reactions that could give rise to inaccurate OraQuick results.
- The studies showed that the OraQuick HCV (using blood, plasma and serum samples) has a very high sensitivity and specificity.
- No safety issues were identified with the OraQuick HCV.

Technical factors

- Sensitivity is slightly lower for oral fluid samples than blood-based samples with the OraQuick HCV. Specificity is comparable for the 2 sample types.
- When using oral fluid sampling, tests should not be done within 15 minutes of a person eating, drinking or chewing gum, or within 30 minutes of using oral care products such as mouthwash or tooth whitener.

Cost and resource use

- The initial cost of the OraQuick HCV is £12 to £15 per single test, depending on the volume purchased.
- No published economic analyses of the OraQuick HCV were identified.

Introduction

The hepatitis C virus (HCV) is a blood-borne virus that predominantly infects liver cells. In

some people HCV infection can lead to cirrhosis of the liver, primary liver cancer or liver failure (Hepatitis C Trust). It is estimated that in 2014, about 214,000 people in the UK had chronic HCV infection (Public Health England 2014) and around half of those are undiagnosed because of long-term asymptomatic infection (NHS Choices 2013).

HCV is usually transmitted through blood-to-blood contact. Around 90% of HCV infections diagnosed in the UK will have been acquired through injecting drugs. Around 50% of people in the UK who have injected drugs have antibodies against HCV (Public Health England, November 2014).

NICE's guidance on promoting and offering testing to people at increased risk of HCV infection identifies the following groups as being at increased risk:

- People who have ever injected drugs.
- People who had a blood transfusion before 1991 or blood products before 1986.
- People born or brought up in a country with a 2% or greater prevalence of chronic hepatitis C.
- Babies born to mothers infected with hepatitis C.
- Prisoners, including young offenders.
- Children and young people living in care homes.
- People living in hostels for the homeless or sleeping on the streets.
- HIV-positive men who have sex with men.
- People in close contact with someone known to be chronically infected with hepatitis C.

This list includes vulnerable people who are difficult to engage in health care. Commonly, people who are tested for HCV lose contact with clinical staff before they can receive their test results.

In the acute phase of HCV infection, symptoms may appear a few weeks after exposure to the virus. Symptoms include: high temperature; tiredness; loss of appetite; stomach pains and nausea; and sometimes jaundice (NHS Choices 2013). Many people infected with HCV have no symptoms, or have only symptoms that are minor and non-specific, so they do not

get tested for HCV or seek treatment. In 20% of people infected with HCV, the immune system will eliminate the virus without any medical care and they will have no further symptoms (unless they become re-infected). In the remaining cases, HCV can persist inside the body for years. This is known as the chronic phase of HCV infection. The symptoms of chronic HCV can vary. Some people have very few symptoms, whereas for others it may significantly affect their quality of life.

Chronic HCV infection is associated with increased risk of irreversible liver damage (cirrhosis) and liver cancer. If HCV infection is detected before serious complications develop, treatments are available. Data from 2006 to 2011 showed that per year in England, only 3% of people with chronic HCV infection started treatment for HCV (PHE July 2014).

Public Health England's recommendations include increasing testing and awareness of HCV to help tackle infection (Public Health England 2014).

Technology overview

This briefing describes the regulated use of the technology for the indication specified, in the setting described, and with any other specific equipment referred to. It is the responsibility of healthcare professionals to check the regulatory status of any intended use of the technology in other indications and settings.

About the technology

CE marking

The CE mark for the OraQuick HCV rapid antibody test as a Class IIa medical device was last updated by OraSure Technologies in October 2013.

Description

The OraQuick HCV is a single-use, point-of-care test for anti-hepatitis C virus (HCV) antibodies. It provides a result in 20 to 40 minutes. The OraQuick HCV can use oral fluid, fingerstick whole blood, venepuncture whole blood, plasma or serum. HCV genotypes 1, 1a,1b, 1a/b, 2, 2a, 2a/c, 3, 3a, 3b, 3a/b, 4, 4a, 4c/d, 4h, 5a and 6a have all been tested by

the manufacturer and are reactive to the OraQuick HCV.

Each test kit contains:

- a pouch containing:
  - the OraQuick HCV rapid antibody test plus absorbent packet
  - an OraQuick HCV developer solution (0.75 ml phosphate buffered saline solution containing polymers and an antimicrobial agent)
- reusable test stands
- collection loops
- package insert.

The manufacturer provides clear and comprehensive instructions for collecting samples of oral fluid, fingerstick whole blood, venepuncture whole blood, serum or plasma for testing using OraQuick. This includes advice for patients. All of the sample preparation processes use standard advice and equipment.

Tests results with the OraQuick HCV are ready in 20 to 40 minutes. If anti-HCV antibodies are detected in the fluid sample, 2 red bands will be visible: 1 at the test line and the other at the control line. If the test sample is negative for anti-HCV antibodies, a red band will be visible at the control line but not at the test line.

The OraQuick HCV test comes with quality control reagents that should be used when the manufacturer specifies:

- when each new operator is using the kit
- whenever a new test kit lot is opened
- whenever a new shipment of kits is received
- whenever the kit storage area falls outside of 2C to 30C (36F to 86F)
- whenever the kit testing area falls outside of 15C to 37C (59F to 99F)
- at periodic intervals dictated by the user facility.

Intended use

The OraQuick HCV is intended for use in people aged 11 years or older who show signs and symptoms that may be due to HCV infection, or who have risk factors for HCV infection.

Setting and intended user

The OraQuick HCV is used at the point of care by health care professionals such as doctors or nurses and, because no specialist equipment is needed, it can be used in any setting.

Current NHS options

Standard testing for anti-HCV antibodies comprises either phlebotomy, in the case of dried-blood spot testing, or a fingerstick blood sample. In both instances, the blood sample is sent to a laboratory where it is tested. Initially, blood is tested by enzyme immunoassay (EIA), also known as enzyme-linked immunosorbent assay (ELISA). The blood sample is added to isolated antigens (in this case, HCV protein fragments) in a plate or well. Any anti-HCV antibodies present in the blood sample bind their target antigen(s). A secondary, enzyme-labelled antibody or antigen is then added, causing a change in colour that can be read visually or quantified by an automatic fluorescence reader.

Laboratory test results are available in about 1 week. A positive result for anti-HCV antibodies shows that the person has been exposed to HCV. This does not mean that they have an active HCV infection, because anti-HCV antibodies will remain in the blood even if the person's immune system has cleared a past infection.

Following a positive test result, either with standard laboratory EIA testing or with the OraQuick HCV, a second laboratory test is needed to test for the presence of HCV infection. This is a reverse transcriptase polymerase chain reaction (RT–PCR) test that detects HCV itself. A positive RT–PCR result indicates an active infection, and a negative result indicates that the patient has been infected in the past but has already cleared the virus.

NICE is aware of the following CE-marked devices that appear to fulfil a similar function to OraQuick HCV:

- Multiplo Rapid HBV/HIV/HCV Antibody Test (Medmira Laboratories): this point-of-care test can be used on fingerstick blood, serum, plasma and whole blood samples but not oral fluid samples.

Costs and use of the technology

The confirmed list price of the OraQuick HCV as of November 2014 is £12–15 (depending on volumes ordered).

The costs for conventional anti-HCV antibody testing are given in table 1. These costs were taken from a health technology assessment (Castelnuovo et al. 2006), and where possible costs were updated using PSSRU 2013 (Curtis 2013).

Table 1 Costs of conventional anti-HCV antibody testing

Item	Cost	Sources/notes
Cost of EIA test	£6.36	Example cost from Worcester Royal Hospital (provided by specialist commentator).
Cost of communicating results if EIA negative	£2.83	Assuming 1 letter to patient and 5 minutes of nurse time (nurse at GP practice, PSSRU 2013) to organise.
Cost of counselling, communicating results and offering referral if EIA positive	£40.83	One letter to patient (£2.83, as above), 1 GP visit to discuss results (10 minute consultation, at £3.80 per minute of patient contact, PSSRU 2013).
Cost of PCR	£113.00	£56.00 for PCR test, £57.00 for 1 specialist consultation (Castelnuovo et al. 2006).

Abbreviations: EIA, enzyme immunoassay; HCV, hepatitis C virus; PCR, polymerase chain reaction.

Likely place in therapy

The OraQuick HCV would be used in place of the existing EIA whole blood test in any setting where people at increased risk of HCV infection are offered testing. This could include primary care such as GP practices, sexual health clinics and mobile street clinics. By providing a rapid result, clinical staff may be able to offer further investigation and

treatment before the person is lost to follow-up.

Specialist commentator comments

One specialist commentator highlighted the test's high specificity, and said that this supported its use as a screening device. However, the commentator noted that the OraQuick HCV lacked sensitivity as a diagnostic test in some studies. Therefore, appropriate confirmatory testing would always be recommended for any patient testing positive using the OraQuick HCV.

One commentator noted that rapid testing, rather than standard laboratory testing of venous blood, could be useful in the event of an HCV outbreak. Another commentator said that the OraQuick HCV could be beneficial as a screening tool, particularly in populations that have infrequent or unreliable contact with the health care system. They also noted that the OraQuick HCV gave people a choice of fluid to be tested.

Two specialists recommended that before use, each OraQuick HCV test should be checked using the quality control reagents provided by the manufacturer. Another noted the importance of checking that the foil packaging is intact prior to testing, and that the test has not passed its expiry date.

One commentator stated that the reduced risk of needlestick injuries would also be a benefit for health care professionals administering the test.

One specialist commentator remarked that the OraQuick HCV does not test for hepatitis B. In some UK areas, a single dried blood spot is used to test for hepatitis B and C. Therefore, this may be missed when testing populations with high prevalence of hepatitis B such as people of Southeast Asian family origin.

Equality considerations

NICE is committed to promoting equality and eliminating unlawful discrimination. We aim to comply fully with all legal obligations to:

- promote race and disability equality and equality of opportunity between men and women
- eliminate unlawful discrimination on grounds of race, disability, age, sex, gender

reassignment, pregnancy and maternity (including women post-delivery), sexual orientation, and religion or belief, in the way we produce our guidance (these are protected characteristics under the Equality Act 2010).

The OraQuick HCV device could be used as part of the diagnosis of HCV in a number of high-risk groups, many of which are protected by the Equality Act 2010. This includes older people, people of South Asian family origin, men who have sex with men, people who inject drugs and people with renal failure or haemophilia. Age, race, sexual orientation and chronic health conditions are protected characteristics under the Equality Act 2010.

Patient and carer perspective

The Hepatitis C Trust gave the following perspectives on the OraQuick HCV test.

In general the OraQuick HCV test was considered to be beneficial over standard testing as it the OraQuick HCV gives an immediate test result. However, this test has the disadvantage of detecting antibodies against HCV and therefore cannot confirm an active virus infection.

People taking the test have more control over the testing procedure, and can sample their own oral fluid, and this leads to less pain, anxiety and clean-up than needlesticks for blood tests. People with compromised veins may experience pain and anxiety whilst the tester identifies a suitable vein to take a venous blood sample. Also people being tested have been fascinated with the simplicity of the test and pleased with the short time taken to give a test result. When people are given a positive OraQuick HCV test result this can provide them a strong motivation to undergo RT-PCR testing to confirm active infection.

The people performing the OraQuick HCV test reflected that this test was a cleaner process as there was no blood waste or risk of blood spills. The people taking the test had no anxiety around the test and therefore had a greater trust and engagement with the tester. The testers found the test to be efficient, reliable and simple to read. They noted that the test is a similar technology to pregnancy tests and therefore the people being tested understood the test process, whereas blood tests needed expert interpretation to understand the results. As the samples were processed at the point of care, there was no need to range for storage or collection of samples and transporting these to the laboratory for testing. This reduced the complexity of the testing process. The HCV trust noted that as the OraQuick HCV test is very simple to use, the test can be performed by people who are not health care professionals.

A health worker who uses OraQuick HCV for testing people from the South Asian community gave their perspective. They noted that within the South Asian community the test had been well received. The test was suitable for Muslim people to use during Ramadan as no part of the test enters the body. Also as no blood is used this makes the test more acceptable at different venues such as Melas and Mosques. The health worker suggested that it would be very useful if the OraQuick HCV tested for Hepatitis B virus as well as HCV.

Evidence review

Clinical and technical evidence

Regulatory bodies

A search of the Medicines and Healthcare Products Regulatory Agency (MHRA) website revealed no manufacturer Field Safety Notices or Medical Device Alerts for this equipment. No reports of adverse events were identified from a search of the Food and Drug Administration (FDA) database: Manufacturer and User Device Facility Experience (MAUDE).

Clinical evidence

Literature searches identified 19 publications, of which 11 were selected as relevant to the OraQuick HCV summarised in this briefing.

The following table gives the range of sensitivity and specificities in all relevant identified studies, from the lowest reported values to the highest.

Table 2 Range of sensitivities and specificities reported in studies summarised in this briefing

–	Sensitivity (%)	Specificity (%)
Oral fluid	90.8 to 99.2	92.1 to 100.0
Whole blood	94.4 to 100.0	98.8 to 100.0
Fingerstick blood	95.9 to 100.0	99.9 to 100.0

–	Sensitivity (%)	Specificity (%)
Serum	99.9 to 100.0	99.8 to 100.0
Plasma	99.4 to 100.0	99.7 to 99.9

The study by Cha et al. (2013) is a diagnostic test accuracy study (using oral fluids with the OraQuick HCV and serum for EIA) from 137 patients diagnosed with hepatitis C and 300 healthy blood donors. Stored serum samples (200 HCV-positive and 200 HCV-negative) were also tested. Sensitivity and specificity data for the OraQuick HCV are reported.

Drobnik et al. (2011) investigated the diagnostic test accuracy study comparing oral fluid OraQuick results with blood EIA testing. There were 503 patients recruited from 6 community-based organisations. Diagnostic performance was not directly reported, but the External Assessment Centre (EAC) which authored the briefing calculated sensitivity and specificity data from data in the publication.

The study by Gao et al. (2014) is a diagnostic test accuracy study, screening a population of patients after nosocomial HCV outbreak. In the study, 1,157 people were tested. Sensitivity, specificity, and positive and negative predictive values are reported.

Hayes et al. (2014) conducted a questionnaire-based study to show patient experience and preference after phlebotomy-based and OraQuick HCV testing. In the study, 129 patients were surveyed about their impressions on test accuracy, pain, waiting times for results and other factors.

The study by Larrat et al. (2012) is a diagnostic test accuracy study, using oral fluid samples and fingerstick blood for the OraQuick HCV compared with dried blood spots for standard EIA testing. Sensitivity, specificity, positive and negative predictive values and likelihood ratios are reported.

The study by Lee et al. (2010) is a diagnostic test accuracy study using oral fluid, serum, plasma, whole venous blood and fingerstick blood. Results were compared with standard laboratory EIA testing. In total, 122 HCV-positive and 450 HCV-negative samples were tested. Sensitivity and specificity data are reported.

Lee et al. (2011) conducted a diagnostic test accuracy study using oral fluid, serum, plasma, whole venous blood and fingerstick blood. Results were compared with standard laboratory EIA testing, which was used to determine the person's HCV status. The study

included 2206 people. Sensitivity and specificity data are reported, as well as potential contaminating factors for the oral sampling, such as food, drink or oral health care products.

The study by Morano et al. (2014) was a survey study of patient experience and preference, comparing OraQuick fingerstick blood testing with standard phlebotomy-based testing. There were 438 patients surveyed. Patient demographics, HCV risk factors and linkage to care are reported.

O'Connell et al. (2013) conducted a laboratory-based diagnostic test accuracy study for military blood donor testing. There were 335 HCV-positive and 339 HCV-negative blood donor plasma specimens tested with the OraQuick HCV. EIA and recombinant immunoblot assay (RIBA) were used as laboratory standard testing. HCV-positive and negative plasma was added to whole blood samples for testing. Sensitivity, specificity and likelihood ratios are reported, as well as the OraQuick HCV's performance under various storage and usage conditions, such as extreme temperatures.

Scalioni et al. (2014) conducted a diagnostic test accuracy study using blood, serum and oral fluid samples from 3 groups: 172 suspected HCV cases, 459 people from a low-risk population and 43 people from a high-risk population. The comparator was laboratory EIA, confirmed by PCR test. Sensitivity, specificity, and positive and negative predictive values are reported.

The study by Smith et al. (2011) is a diagnostic test accuracy study of people from 4 different cities who inject drugs. The OraQuick HCV was tested with oral fluid and fingerstick blood. Two reference standards were used: EIA and RIBA. Sensitivity, specificity, and true and false positives and negatives were reported.

Included studies are summarised in tables 3 to 13.

Table 3 Overview of the Cha et al. 2013 study

Study component	Description
Objectives/ hypotheses	To assess the diagnostic performance of the OraQuick HCV compared to standard laboratory methods.
Study design	Diagnostic test accuracy.

Study component	Description
Intervention	The OraQuick HCV using either serum or oral fluid.
Setting	2 Korean hospitals: Samsung Medical Centre and Seoul National University Bundang Hospital.
Inclusion/ exclusion criteria	People who were previously diagnosed with HCV on the basis of clinical and laboratory tests. The publication did not report whether this diagnosis was from antibody testing or RT–PCR.
Primary outcomes	Clinical sensitivity and specificity, analytical sensitivity, interference and cross-reactivity.
Methods	Comparator laboratory tests: Architect (Abbott) AxSYM (Abbott), E170 (Roche), ADVIA Centaur (Siemens) and Elecsys (Roche). A total of 3 other rapid tests were also used as comparators: Asan Easy Test HCV (Asan Pharmaceutical), SD BIOLINE HCV (SD), Genedia HCV Rapid LF (Green Cross Medical Science). For the OraQuick HCV, oral fluid and serum samples were tested. After oral fluid testing, venous blood samples were drawn. Sera could only be obtained in 114 patients enrolled in the oral fluid test. If oral test result in these HCV-positive patients was unreactive, the OraQuick HCV with oral fluid was repeated, and the serum was tested using Architect EIA (Abbott). An additional 200 HCV–RNA-positive serum samples from a blood bank were also tested. In healthy blood donors, all oral fluids were tested at the site of blood donation. If the oral test was unreactive, it was immediately repeated using the OraQuick HCV. All results were compared to serum Architect EIA (Abbott). If there was a discrepancy in the results, the Architect EIA serum test was repeated and confirmed by Western blot (HCV Blot 3.0, MP Biomedicals) and HCV RT–PCR (COBAS). AmpliPrep/COBAS TaqMan HCV Test 2.0, Roche Diagnostics). An additional 200 HCV-negative serum samples from a blood bank were also tested.
Participants	There were 137 previously diagnosed HCV-positive oral fluid samples. There were 114 serum samples from the same patients. There were 300 healthy-patient samples for specificity.

Study component	Description
Experience of person undertaking test	Not reported.
Results	Oral fluid sensitivity 95% CI, 97.8 (93.2 to 99.4) [134/137]. Oral fluid specificity 95% CI, 100.0 (98.4 to 100.0) [300/300]. Serum sensitivity 95% CI, 100 (97.7 to 100.0) [200/200]. There were 3 false negatives: all patients who previously had HCV but were treated with antivirals. RNA was not detected in 2 of these patients (no active infection). Dilution tests: Dilution tests showed that the OraQuick HCV was 'quite comparable' to laboratory assays such as Architect, Centaur, AxSYM. HCV genotype sensitivity: HCV genotypes 1a, 2b and 3a tested. The OraQuick HCV was more sensitive with genotype 3a panel – detected anti-HCV antibodies 10 days earlier than Architect and E170 did. Interference and cross-reactivity: Neither bilirubin (up to 171 µmol/l), haemoglobin (5 g/l) nor triglycerides (up to 3.39 mmol/l) showed any interference. No cross reactivity with sera positive for rheumatoid factor, multipara, other viral infections such as HIV, hepatitis A or B.
Adverse events	None
Conclusions	Clinical performance of the OraQuick HCV is comparable to laboratory-based assays with both serum and oral fluid. This supports the supplementary use of rapid HCV testing using oral fluid in various medical and non-medical settings.

Abbreviations: CI, confidence interval; EIA, enzyme immunoassay; HCV, hepatitis C virus; RNA, ribonucleic acid; RT–PCR, reverse transcriptase polymerase chain reaction.

Table 4 Overview of the Drobnik et al. 2011 study

Study component	Description
Objectives/ hypotheses	To evaluate the accuracy of the OraQuick HCV and assess its feasibility for use by community-based organizations in the USA for high HCV-risk populations.
Study design	Diagnostic test accuracy.
Intervention	The OraQuick HCV using oral fluid.
Setting	Six community-based organizations in the USA.
Inclusion/ exclusion criteria	People aged 18 years or older who consented in English, Spanish or French, have a self-reported history or at least 1 of the following risk factors: injecting drug use, incarceration, HIV infection, sexually transmitted infection, liver disease, receipt of a blood transfusion or clotting factor before 1992, organ transplantation, haemodialysis, non-licensed tattoo or piercing, and sexual partners who were injecting drug users or HCV-positive.
Primary outcomes	OraQuick/EIA results concordance, clinical staff impressions of the technology.
Methods	Oral fluid samples were taken as per the manufacturer's instruction and processed at the point of care. Blood samples were sent away for reference testing using Abbott HCV EIA 2.0 (Abbott) testing. If the signal-to-cut-off ratio from EIA was between 1 and 3.8 (low signal), the laboratory performed a recombinant immunoblot assay (Chiron RIBA HCV 3.0 Strip Immunoblot Assay, Chiron).
Participants	There were 503 patients from 6 community-based organisations recruited between April and September 2009.

Study component	Description
Experience of person having test	Researcher questionnaire: The OraQuick HCV preferred for use in 98.5% of client visits. Staff more likely to recommend the OraQuick HCV over blood test as phlebotomy is difficult in community centres. Patients are concerned about having to come back for HCV test results, so single rapid test is preferred. Single visit means more referrals for PCR tests and medical care. Reduced risk of needlestick injury for staff. Rapid testing may allow higher volume of testing.
Results	Specimens from 486 patients (96.6%) provided valid results. From the OraQuick HCV and EIA comparator. The OraQuick HCV and EIA yielded the same result in 474 (97.5%) patients. EAC calculated diagnostic performance (from data in the publication). Sensitivity, 93.88% Specificity, 99.48% Discordant OraQuick/EIA tests resolved using PCR: Study results were discordant for 12 patients (2.5%). PCR testing could not be performed on 2 of these patients because sample volume was not sufficient. In 10 discordant results, PCR testing confirmed the OraQuick result in 6 cases (indicating active infection); PCR confirmed the EIA result in 1 case (indicating active infection) and the remaining 3 results were either invalid or indeterminate for OraQuick or EIA.
Adverse events	None
Conclusions	OraQuick accuracy is comparable to EIA comparator. The oral swab rapid test could help HCV screening programs reach individuals unaware of their status and expand.

Abbreviations: HCV, hepatitis C virus; EIA, enzyme immunoassay; PCR, polymerase chain reaction.

Table 5 Overview of the Gao et al. 2014 study

Study component	Description
Objectives/ hypotheses	To assess the use of the OraQuick HCV as a screening tool in the case of HCV outbreak.
Study design	Diagnostic test accuracy (screening).
Intervention	The OraQuick HCV using either serum or whole blood.
Setting	USA. Outbreak of HCV in a cardiac catheterization laboratory, from an infected healthcare worker.
Inclusion/ exclusion criteria	Patients treated during the period of the infected healthcare worker's employment were asked to present to 1 of 8 emergency public health clinics for HCV testing.
Primary outcomes	Sensitivity, specificity, and positive and negative predictive value.
Methods	Patients were informed by phone call and letter to present to 1 of 8 public clinics. Two serum samples (for EIA reference and additional tests if needed), and 1 whole blood sample (for the OraQuick HCV) were collected for each patient. OraQuick results were given on-site; serum samples were sent away for laboratory testing. Any specimen that was positive or invalid was retested on-site by a blinded second tester, who was unaware that it was a repeat test. Once confirmed, results were relayed to the patient. Comparator: Ortho HCV v3.0 EIA (Ortho Clinical Diagnostics). Discordant results were frozen at -70C and sent for chemilluminescent assay testing at the US Centers for Disease Control and Prevention. Positive results (by the OraQuick HCV or EIA) also tested for HCV RNA by Cobas Amplicor HCV test v2.0 (Roche).
Participants	1,174

Study component	Description
Results	There were 22 positives (1.9%), 1,134 negatives (98.0%) and 1 invalid result (0.1%). OraQuick sensitivity, 94.4% Specificity, 99.4% PPV, 72.7% NPV, 99.9% Six OraQuick positives were negative by EIA and CIA, 1 negative OraQuick was positive by EIA and CIA. All were negative by RT–PCR for HCV RNA (indicating no active infection present).
Adverse events	None reported
Conclusions	Demonstrates that the OraQuick HCV can be used in an outbreak setting to allow rapid screening of a large number of patients. This can identify HCV-infected patients who may be counselled and prevent further spread of the disease. The OraQuick HCV could be integrated into future HCV outbreak testing algorithms.

Abbreviations: CIA, chemilluminescent; EIA, enzyme immunoassay; HCV, hepatitis C; SCR, signal to cut off ratio; RNA, ribonucleic acid; RT–PCR, reverse transcriptase polymerase chain reaction.

Table 6 Overview of the Hayes et al. 2014 study

Study component	Description
Objectives/ hypotheses	To assess the preference and acceptability of the OraQuick HCV against standard anti-HCV antibodies testing in injecting drug users, at high risk of HCV infection.
Study design	Questionnaire study.
Intervention	The OraQuick HCV using fingerstick blood.
Setting	San Francisco, USA. Questionnaire following up patients tested with both OraQuick (fingerstick blood only) and phlebotomy-based testing.

Study component	Description
Inclusion/ exclusion criteria	People who had injected drugs in the last 30 days, aged over 30 years, who previously completed a baseline visit. Must self-report negative or unknown HCV RNA status, or prospective patients with unknown HCV status, or anti-HCV antibodies positive but HCV RNA negative.
Primary outcomes	Testing preference (rapid or standard), participant demographics/ characteristics, comparison with phlebotomy-based testing from patient perspective.
Methods	Eligible patients asked to complete HCV rapid test acceptability survey. Frequencies and measures of central tendency were used to describe sample characteristics and perception of HCV rapid testing (preferences, perceptions and reasons for testing choice). All patients participating had phlebotomy and OraQuick test (fingerstick blood only), regardless of testing method selection.
Participants	129

Study component	Description
Results	98.4% (127/129) completed the survey. 82.9% (n=107) chose the rapid test over standard HCV testing using phlebotomy. 60.2% (50/83) chose it because of rapid results. 84.4% (81/96) preferred getting their results on the same day, and 97.5% (94/96) understood their results. Note: Reasons for missing responses include interviewer error (n = 13) and a faulty skip pattern (corrected early in data collection) in which participants who preferred standard anti-HCV testing were not asked a follow-up question regarding testing preference reason (n = 7). 60.5% (78/129) felt the rapid test was at least as accurate as standard testing. 53.5% (53/99) thought it was less painful than tests involving venepuncture. 93.9% (92/98) would recommend this test to a friend. 3.1% (3/97) thought it would be better to wait a week to get lab samples back instead. Of the patients who opted for the standard lab test, 38.1% (8/21) felt that the older test was more established and therefore reliable. 14.3% (3/21) did not want their test results on that day, and felt the standard HCV test was more convenient. A total of 9.5% (2/21) were afraid of having a finger pricked and 4.8% (1/21) felt that the standard test was less painful. Overall, 13.2% (17/129) felt that the OraQuick HCV was to some degree less accurate.
Adverse events	None
Conclusions	OraQuick test by finger-prick is more widely accepted by people who inject drugs than phlebotomy-based testing.

Table 7 Overview of the Larrat et al. 2012 study

Study component	Description
Objectives/ hypotheses	Evaluation of a commercially available EIA and OraQuick with fingerstick blood and oral mucosal transudate (OraQuick results only reported in this table).
Study design	Diagnostic test accuracy.

Study component	Description
Intervention	The OraQuick HCV with fingerstick blood and oral mucosal transudate.
Setting	Hepatology or infectology units of Grenoble University Hospital, France.
Inclusion/ exclusion criteria	Not reported, HCV-positive and HCV-negative patients recruited from the hospital units (see above).
Primary outcomes	Sensitivity, specificity, storage conditions of dried blood spots and oral mucosal transudate on test performance.
Methods	For each patient, 2 oral samples were taken (1 for the OraQuick HCV, 1 for EIA). The order of each sample being taken was randomized, with 10 minutes between each. Fingerstick blood was placed alternatively on the OraQuick Sample loop or onto Protein Saver 903 card for dried blood spot samples (dried for 24 hours, stored at -20C). Comparator EIA: Monolisa HCV–Ag–Ab–ULTRA (BioRad). EIA results from serum samples taken at recruitment used as baseline.
Participants	113 HCV-positive people consecutively recruited between May and September 2011; 88 HCV-negative people also sampled during this time.
Experience of person having test	Not reported.

Study component	Description
Results	Diagnostic performance: **Fingerstick blood** Sensitivity 95% CI, 97.4 (92.5 to 99.1) Specificity 95% CI, 100 (95.8 to 100) PPV, 100 NPV, 96.2 LR+ve, Infinity LR–ve, 0.03 **Oral fluid** Sensitivity 95% CI, 94.6 (88.6 to 97.5) Specificity 95% CI, 100 (95.7 to 100) PPV, 100 NPV, 92.5 LR+ve, Infinity LR–ve, 0.05 Of the fingerstick blood samples, 1 false-negative correlated with spontaneously-resolved HCV infection with low cEIA index value (1.70) in serum. There were 2 others that were HCV RNA-negative, HIV-positive.
Adverse events	None reported.
Conclusions	Commercial EIA can be used on stored samples as a reliable alternative to OraQuick point-of-care testing.

Abbreviations: cEIA, commercial enzyme immunoassay; CI, confidence interval; EIA, enzyme immunoassay; HCV, hepatitis C virus; LR, likelihood ratio; NPV, negative predictive value; PPV, positive predictive value; RNA, ribonucleic acid.

Table 8 Overview of the Lee et al. 2010 study

Study component	Description
Objectives/ hypotheses	To evaluate the performance of the OraQuick HCV with venous blood, fingerstick blood, serum, plasma, and oral fluid, compared with FDA-approved laboratory methods.
Study design	Diagnostic test accuracy.
Intervention	The OraQuick HCV using venous blood, fingerstick blood, serum, plasma, and oral fluid.
Setting	Not reported.
Inclusion/ exclusion criteria	Not reported.
Primary outcomes	Sensitivity, specificity, factors predictive of false-positive and false-negative test results.
Methods	People with HCV infection (n=122) and at low-risk of HCV infection (n=450) samples (oral fluid, venous whole blood, fingerstick blood, plasma and serum) tested with the OraQuick HCV and comparator tests. Comparators: EIA (make/manufacturer not named), RIBA strip immunoblot assay. A positive HCV diagnosis was made when there was a positive EIA and RIBA, or a positive EIA and PCR. Sensitivity to anti-HCV antibodies seroconversion was tested in 19 commercially-available panels of plasma specimens sequentially collected from individuals having HCV seroconversion following recent infection.
Participants	122 HCV-positive people and 450 low HCV-risk people, of unknown HCV status.

Study component	Description
Results	121/122 (99.2%) detected by the OraQuick HCV. There was 1 case that tested negative in oral fluid but positive in all other samples. The serum from this individual was positive on EIA and RIBA but PCR-negative. There were 449/450 (99.8%) correctly identified as HCV negative by the OraQuick HCV. There was 1 patient whose sample gave a false positive (RIBA and PCR negative) and 1 low-risk patient correctly identified as HCV positive by the OraQuick HCV, confirmed by control tests. Oral fluid sensitivity 95% CI, 99.2% (95.5 to 100) Oral fluid specificity 95% CI, 100% (99.2 to 100) Venous whole blood sensitivity 95% CI, 100% (97.0 to 100) Venous whole blood specificity 95% CI, 100% (99.2 to 100) Fingerstick blood sensitivity 95% CI, 100% (97.0 to 100) Fingerstick blood specificity 95% CI, 100% (99.2 to 100) Plasma sensitivity 95% CI, 100% (97.0 to 100) Plasma specificity 95% CI, 99.8% (98.8 to 100) Serum sensitivity 95% CI, 100% (97.0 to 100) Serum specificity 95% CI, 99.8% (98.8 to 100) Mean time to detection of seroconversion was 61.3 days in EIA and 56.4 days in the OraQuick HCV. Of 19 seroconversion panels tested, HCV antibody was detected at the same time by the OraQuick HCV and EIA in 9 cases and earlier by the OraQuick HCV in 10. In no cases did EIA detect before the OraQuick HCV. EAC diagnostic performance calculations: HCV-positive people Sensitivity (%), 99.18 PPV (%),100.00, NPV (%), 0.00 Low-risk people Sensitivity (%), 100.00; Specificity (%), 99.78 PPV (%), 50.00; NPV (%), 100.00; LR (+ve), 449.0; LR (−ve), 0.00

Study component	Description
	This study had separate 2×2 tables within the publication, as they sampled HCV-positive people in 1 group and low-risk HCV-status-unknown people in another. These were kept separated, as they do not reflect population prevalence in a real-world scenario.
Adverse events	None reported.
Conclusions	The OraQuick HCV appears to have a sensitivity and specificity equivalent to laboratory-based tests, even when antibody levels are low, and is suitable as an aid in the diagnosis of HCV infection.

Abbreviations: CI, confidence interval; EIA, enzyme immunoassay; HCV, hepatitis C virus; PCR, polymerase chain reaction; RIBA, recombinant immunoblot assay.

Table 9 Overview of the Lee et al. 2011 study

Study component	Description
Objectives/ hypotheses	To evaluate the prospective diagnostic performance of the OraQuick HCV with venous blood, fingerstick blood, serum, plasma, and oral fluid, compared to FDA-approved laboratory methods, in HCV-at-risk people.
Study design	Diagnostic test accuracy.
Intervention	The OraQuick HCV using venous blood, fingerstick blood, serum, plasma, and oral fluid.
Setting	8 separate clinical testing sites, otherwise not reported.
Inclusion/ exclusion criteria	People at risk of HCV infection, or who had signs and/or symptoms of HCV infection. Risk factors included: had injected intravenous drugs; born to HCV-positive mother; had sex with known HCV-positive partner; had sex with more than 2 different sexual partners in the last 6 months; had sex with an intravenous drug user; currently have or ever had a sexually transmitted disease; have been on long-term haemodialysis; HIV-positive; had a blood transfusion, blood product or organ transplant prior to 1992; have been incarcerated.

Study component	Description
Primary outcomes	Sensitivity, specificity, interference factors for oral testing.
Methods	There were 2,206-HCV positive and low-risk HCV samples tested with the OraQuick HCV and comparator tests (venous blood, fingerstick blood, serum, plasma, and oral fluid). Each sample type was tested for each patient in an unblinded fashion. Comparators: EIA (Abbott AxSym); RIBA (Chiron); PCR (COBAS); AMPLICOR Hepatitis C Virus Test v2.0 (Roche). People were diagnosed HCV-positive with both positive EIA and positive RIBA, or positive EIA and positive PCR. Oral interference study: There were 50 HCV-negative samples collected and tested under the following conditions: gingivitis present, use of dentures, consumption of food or beverage, use of tobacco products, use of oral care products (tooth brushing, mouthwash, and tooth whitening). Specimens were tested 5, 10, 15 and 30 minutes post-exposure to the interfering condition. Seroconversion panel study: Sensitivity to anti-HCV antibodies seroconversion was tested in 27 commercially-available panels of plasma specimens sequentially collected from individuals having HCV seroconversion following recent infection.
Participants	There were 2,206 people at risk of HCV and/or with signs or symptoms of hepatitis who took part. Of these, 123 (5.6%) had symptoms of hepatitis and 1,930 (87.5%) were asymptomatic.

Study component	Description
Results	**Sensitivity and specificity** There were 2,183 people classed as HCV-positive (757, 34.3%) or HCV negative (1,426, 64.6%). In total 23 were excluded due to indeterminate RIBA test and negative PCR. Sensitivities (99.7 to 99.9%) for venous blood, fingerstick blood, serum and plasma. Lower (98.1%) in oral fluid. Specificities were equivalent (99.6 to 99.9%) for all sample types. **Oral fluid** Sensitivity 95% CI, 98.1% (96.9 to 99.0) [739/753] Specificity 95% CI, 99.6% (99.2 to 99.9) [1418/1423] PPV, 99.33%; NPV, 99.02%; LR+ve, 279.31; LR–ve,0.02 **Venous whole blood** Sensitivity 95% CI, 99.7% (99.9 to 100.0) [753/755] Specificity 95% CI, 99.9% (99.5 to 100.0) [1421/1423] PPV, 99.74%, NPV, 99.86 %, LR+ve, 709.62; LR–ve=0.00 **Fingerstick blood** Sensitivity 95% CI, 99.7% (99.0 to 100.0) [752/754] Specificity 95% CI, 99.9% (99.6 to 100.0) [1421/1422] PPV, 99.87%; NPV, 99.86 %; LR+ve, 1418.23; LR–ve=0.00 Plasma sensitivity 95% CI, 99.9% (99.3 to 100.0) [755/756] Plasma specificity 95% CI 99.9% (99.5 to 100.0) [1420/1422] PPV, 99.74%; NPV, 99.93%; LR+ve, 711.06; LR–ve, 0.00 Serum sensitivity 95% CI, 99.9% (99.3 to 100.0) [756/757] Serum specificity 95% CI, 99.9% (99.6 to 100.0) [1422/1423] PPV, 99.87%; NPV, 99.93%; LR+ve, 1421.12; LR–ve, 0.00 (PPV, NPV and LRs calculated by EAC from raw data using 2×2 tables) **Oral interference study** Consumption of tobacco and most types of food and drink did not affect results, even at the shortest wait time of 5 minutes. A low rate of false positives at the shortest wait times (5 minutes) after use of mouthwash, whitening products, tooth brushing or acidic drinks (such as cola), but this was not observed with 15 minutes (cola) or 30 minutes (oral care

Study component	Description
	products). **Seroconversion panel study:** HCV antibody detected at the same time by the OraQuick HCV and EIA in 19/27 seroconversion series. The OraQuick HCV detected the anti-HCV antibodies earlier than EIA in 6 cases and the EIA detected earlier in 2 cases. Overall, the OraQuick HCV detected the antibodies 0.6 days (CI 0.1 to 1.4) days before EIA. In no series was there a large difference in seroconversion sensitivity between the OraQuick HCV and EIA (maximum 7 days).
Adverse events	None reported.
Conclusions	The OraQuick HCV demonstrated clinical performance equivalent to laboratory-based tests, and is suitable as an aid in the diagnosis of HCV infection.

Abbreviations: CI, confidence interval; EIA, enzyme immunoassay; HCV, hepatitis C virus; PCR, polymerase chain reaction; RIBA, recombinant immunoblot assay.

Table 10 Overview of the Morano et al. 2014 study

Study component	Description
Objectives/ hypotheses	To evaluate the use of the OraQuick HCV to screen vulnerable individuals; and linkage to care in a mobile medical clinic.
Study design	Diagnostic screening/demographic study.
Intervention	The OraQuick HCV using fingerstick blood.
Setting	Mobile medical clinic in New Haven, Connecticut, USA (March 2012 to March 2013).
Inclusion/ exclusion criteria	Not reported – clients reporting to mobile medical clinic during the time period.

Study component	Description
Primary outcomes	Examine difference between clients who preferred point-of-care testing compared with phlebotomy HCV testing. Multivariate logistic models for 2 outcomes: acceptance of HCV testing and preferring point-of-care testing over phlebotomy. Linkage of specialty HCV care among those testing positive using the 2 diagnostic strategies.
Methods	People were offered either: • standard phlebotomy testing, which tests for hepatitis A, B and C, HIV and syphilis with results in 1 week, or • rapid fingerstick OraQuick testing with immediate results in 20 minutes. Everyone who had a positive HCV antibody tests had blood drawn for confirmatory HCV RNA testing (RT–PCR).
Participants	Clients accepting HCV screening at the mobile medical clinic. patients from 'vulnerable neighbourhoods'.
Results	In total 438/1345 (32.6%) people accepted HCV screening. Of these, 209/438 (47.7%) people chose point-of-care testing (the OraQuick HCV) and 27/438 (6.2%) people had a positive test result for anti-HCV antibodies. No difference in HCV prevalence was detected between point-of-care and standard phlebotomy groups (7.7 compared with 4.8%; p=0.219). Of the patients with a positive anti-HCV antibody test (detected using gold-standard screening or the OraQuick HCV), people who chose the OraQuick HCV were significantly more likely to be linked to HCV specialty care (93.8 compared with 18.2%; p<0.0001).
Adverse events	None reported.
Conclusions	Rapid point-of-care testing is acceptable in a mobile clinic setting, and was preferred by almost half of the people who had HCV screening. patients who selected the OraQuick HCV were statistically significantly more likely to be linked to HCV specialty care.

Abbreviations: EIA, enzyme immunoassay; HCV, hepatitis C virus; RT–PCR, reverse transcriptase polymerase chain reaction; RNA, ribonucleic acid.

Table 11 Overview of the O'Connell et al. 2013 study

Study component	Description
Objectives/ hypotheses	To evaluate the diagnostic performance of the OraQuick HCV and 4 other rapid point-of care tests for emergency testing of blood transfusions in a military setting (OraQuick results only shown here).
Study design	Diagnostic test accuracy.
Intervention	The OraQuick HCV using donor plasma samples.
Setting	Military research laboratory.
Inclusion/ exclusion criteria	HCV-positive and negative plasma samples, also whole blood to which with HCV-positive and HCV-negative plasma had been added.
Primary outcomes	Sensitivity, specificity, performance under stress conditions (for example extreme temperatures).

Study component	Description
Methods	Samples of HCV-positive plasma provided by American Red Cross. Samples of HCV Negative plasma provided by Robertson Blood Centre. Pathogen-free whole blood sourced from Biological Speciality Corporation. Comparator: samples were deemed HCV-positive if the EIA signal-to-cut-off ratio was at least 1 and the RIBA result was positive. **Whole blood testing** Stress conditions: Normal; 18 to 30C • Hot storage; devices stored for 30 days at 57C. Testing performed at 18 to 30C • Hot testing; normal storage conditions (18 to 30C), testing performed at 49C • Cold storage: devices stored for 30 days at -20C. Testing performed at 18 to 30C **Seroconversion panel study** • A total of 54 samples from 5 seroconversion panels were tested. Comparator: HCV EIA v3.0 (Ortho Diagnostics). **User survey:** Ease of use was evaluated by technicians and observers who were using the device. There were 6 questions devised, each on a 5-point Likert scale (1=very difficult; 2=difficult; 3=neither; 4=easy; 5=very easy). • Overall ease of use. • Were the manufacturer's directions straightforward to follow? • Learning how to perform the test (was it easy for you to learn how to perform this test, would it be easy to train others how to perform this test). • Interpreting the test (deciding whether the test is positive or negative

Study component	Description
	based on lines). • Reading the test result (was it easy or difficult to read the lines, was the line dark enough). • Reading the test result within the correct time period.
Participants	There were 335 HCV-positive and 339 HCV-negative blood donor plasma specimens. Pathogen-free whole blood also spiked with HCV-positive (n=84) and HCV-negative (n=84) plasma.
Experience of person having test	Not reported.

Study component	Description
Results	Sensitivity and specificity: Sensitivity 95% CI, 99.4% (98.0 to 99.9) Specificity 95% CI, 99.7% (98.6 to 100.0) Positive likelihood ratio 95% CI, 336.9 (47.6 to 2385.4) Negative likelihood ratio95% CI, 0.01 (0.00 to 0.02) **Whole blood testing** **Normal conditions** Sensitivity 95% CI, 98.8 (94.3 to 99.9) Specificity 95% CI, 98.8 (94.3 to 99.9) LR +ve 95% CI, 83.0 (11.8 to 582.5) LR –ve 95% CI, 0.01 (0.00 to 0.08) **Hot storage** Sensitivity 95% CI, 97.6 (92.4 to 99.6) Specificity 95% CI, 100 (96.5 to 100) LR –ve 95% CI, 0.02 (0.01 to 0.09) **Hot testing** Sensitivity 95% CI, 97.6 (92.4 to 99.6) Specificity 95% CI, 100 (96.5 to 100) LR –ve 95% CI, 0.02 (0.01 to 0.09) **Cold storage** Sensitivity 95% CI, 97.6 (92.4 to 99.6) Specificity 95% CI, 100 (94.5 to 100) LR –ve 95% CI, 0.02 (0.01 to 0.09) **Seroconversion panel study** The OraQuick HCV was 1 of 2 rapid tests that demonstrated the best performance and most consistency with the reference standard. **User survey:** The OraQuick HCV was rated a maximum score of 5 for all survey questions.
Adverse events	None reported.

Study component	Description
Conclusions	The data support OraQuick HCV superiority over the other rapid tests.

Abbreviations: CI, confidence interval; EIA, enzyme immunoassay; HCV, hepatitis C virus; NLR, negative likelihood ratio; PCR, polymerase chain reaction; PLR, positive likelihood ratio; RIBA, recombinant immunoblot assay.

Table 12 Overview of the Scalioni et al. 2014 study

Study component	Description
Objectives/ hypotheses	Evaluate performance of rapid tests for anti-HCV antibodies detection in sera, whole blood and oral fluid samples from individuals with different endemicity profiles and risk behaviours.
Study design	Diagnostic test accuracy.
Intervention	The OraQuick HCV in serum, whole blood and oral fluid samples.
Setting	Brazil, field samples: Group 1: from a viral hepatitis ambulatory clinic in Rio de Janeiro Group 2: remote areas in northern and mid-west regions of Brazil (Tocantins and Mato Grosso do Sul states) Group 3: people from southeast and northeast regions of Brazil who use crack cocaine and beauty professionals living in Rio de Janeiro state.
Inclusion/ exclusion criteria	Group 1: people aged 18 years or older, who read and signed the consent form, and who were either symptomatic or asymptomatic for hepatitis but had at least 1 risk factor (history of intravenous drug use; sexual intercourse with a known carrier of HCV; sexually transmitted disease; long-term haemodialysis; surgery or blood transfusion before 1994; or piercing). Also the inclusion of 120 individuals for blood/serum samples in OraQuick testing. Group 2: people who read and signed the consent form, or whose parents or legal guardians read and signed consent form. Group 3: people who had used crack cocaine within the last 12 months. Beauty professionals (manicurists, pedicurists or hairdressers) who had worked in the last 30 days.

Study component	Description
Primary outcomes	Sensitivity, specificity, reproducibility, cross-reactivity with other infectious agents.
Methods	Field samples: comparator EIA: HCV Ab (Radim) used to test serum samples, confirmed by COBAS AMPLICOR HCV Test 2.0 (Roche Diagnostics). HCV RNA-reactive samples genotyped using Versant HCV Genotype Assay 2.0 (Siemens). The OraQuick HCV was tested with 120 paired serum, whole blood and oral fluid samples, evaluated under laboratory conditions. Whole blood and serum samples collected by venepuncture. Oral fluid collected by the OraQuick HCV swab. OraQuick result read after 40 minutes.
Participants	Group 1: 172 suspected cases sampled Group 2: 459 low-risk individuals Group 3: 43 high-risk individuals (people who use crack cocaine)

Study component	Description
Results	Oral fluid testing: Sensitivity, specificity and other diagnostic performance: **Anti-HCV antibody positive** Sensitivity 95% CI, 88.52 (81.5 to 93.58) Specificity 95% CI, 100 (92.89 to 100) PPV 95% CI, 100 (96.64 to 100) NPV 95% CI, 78.13 (66.03 to 87.49) Kappa statistic, 81.77 (72.62 to 90.29) **HCV RNA positive** Sensitivity 95% CI, 95.35 (88.52 to 98.72) Specificity 95% CI, 100 (92.89 to 100) PPV 95% CI, 100 (95.6 to 100) NPV 95% CI, 92.59 (82.11 to 97.94) Kappa statistic, 93.78 (87.77 to 99.79) **Diagnostic performance in high risk** (Group 3, n=43): TP, 0 TN, 43 FP, 0 FN, 0 **Diagnostic performance in low prevalence** (Group 2, n=459): TP, 0 TN, 455 FP, 0 FN, 4 **Blood testing** **Serum** Sensitivity 95% CI, 100 (95.55 to 100) Specificity 95% CI, 100 (90.97 to 100 PPV 95% CI, 100 (95.55 to 100) NPV 95% CI, 100 (90.97 to 100)

Study component	Description
	Kappa statistic,100 **Whole blood** Sensitivity 95% CI, 98.77 (93.31 to 99.97) Specificity 95% CI, 100 (90.97 to 100) PPV 95% CI, 100 (95.49 to 100) NPV 95% CI, 97.5 (86.84 to 99.94) Kappa statistic, 98.1 **Whole blood** Sensitivity 95% CI, 97.53 (91.36 to 99.70) Specificity 95% CI, 100 (90.97 to 100) PPV 95% CI, 100 (95.44 to 100) NPV 95% CI, 95.12 (83.47 to 99.40) Kappa statistic, 96.25
Adverse events	None reported.
Conclusions	The OraQuick performed the best (of all rapid tests) using oral fluid samples from low-prevalence individuals. It did not perform as well as BioEasy (a different rapid test) in high-prevalence individuals, using whole blood. All rapid tests could be used to identify active HCV infection among individuals from different backgrounds and risk profiles.

Abbreviations: CI, confidence interval; EIA, enzyme immunoassay; FN, false negative; FP, false positive; TN, true negative; TP, true positive; PPV, positive predictive value; NPV, negative predictive value; HCV, hepatitis C virus; PCR, polymerase chain reaction; RNA, ribonucleic acid.

Table 13 Overview of the Smith et al. 2011 study

Study component	Description
Objectives/ hypotheses	To assess the diagnostic performance of 3 rapid, POC anti-HCV antibodies assays compared to standard laboratory methods (data presented here for OraQuick only).

Study component	Description
Study design	Diagnostic test accuracy.
Intervention	OraQuick using either fingerstick blood or oral fluid.
Setting	Community-based HIV and HCV testing. Two of 21 US cities participating in the National HIV Behavioural Surveillance System (NHBS) studied OraQuick (New York City and Seattle).
Inclusion/ exclusion criteria	People who inject drugs (in the last 12 months), aged 18 years or over, living in the participating metropolitan statistical area, who consented to participate and who could complete a survey in English or Spanish.
Primary outcomes	Sensitivity, specificity, factors predictive of false-positive and false-negative test results.
Methods	The reference standard was FDA-approved, laboratory immunoassays according to local study protocols. Positive anti-HCV antibodies specimens were then confirmed with a third-generation recombinant immunoblot assay. Two reference standards were used: Screening assay used as per manufacturer's recommendation: CDC-recommended algorithm.
Participants	The entire cohort size (3 index technologies) was 1861 patients. Results for the OraQuick HCV are available for 816 tests in 550 patients: of either blood (266 tests in 266 patients in Seattle only) or saliva (550 tests in 550 patients in New York and Seattle).

Study component	Description
Results	False-positive or false-negative results were not associated with HIV status, gender or birth year. Use of the CDC reference standard criteria resulted in slightly higher sensitivity across the test, but not statistically significantly so. **New York City (oral)** SA (n=285) Sensitivity 95% CI, 94.4 (90.4 to 96.8) Specificity 95% CI, 95.8 (88.5 to 98.6) PPV, 98.6; NPV, 85.7 LR+ve, 23.7; LR−ve, 0.06 CDC (n=285) Sensitivity 95% CI, 94.7 (90.8 to 97.0) Specificity 95% CI, 92.1 (83.8 to 96.3) PPV, 97.2; NPV, 86.2 LR+ve, 12.8; LR−ve, 0.06 **Seattle (oral)** SA (n=265) Sensitivity 95% CI, 90.8 (85.4 to 93.7) Specificity 95% CI, 98.6 (92.4 to 99.8) PPV, 100; NPV, 78.8 LR+ve, N/A; LR−ve, 0.09 CDC (n=264) Sensitivity 95% CI, 92.2 (87.5 to 95.2) Specificity 95% CI, 97.2 (90.9 to 99.3) PPV, 98.5; NPV, 81.8 LR+ve, 25.7 LR−ve, 0.09 **Seattle (fingerstick blood)** SA (n=266) Sensitivity 95% CI, 95.9 (91.6 to 97.6) Specificity 95% CI, 100 (94.9 to 100.0) PPV=100; NPV=89.7 LR+ve, N/A; LR-ve, 0.04 CDC (n=265) Sensitivity 95% CI, 97.4 (94.1 to 98.9) Specificity 95% CI, 98.6 (92.9 to 99.8) PPV, 100; NPV, 93.1 LR+ve, N/A; LR−ve, 0.03

Study component	Description
Adverse events	None reported.
Conclusions	The authors reported considerable variability in diagnostic performance across sites.

Abbreviations: CI, confidence interval; CDC, US Centers for Disease Control and Prevention; FDA, US Food and Drug Administration; HCV, hepatitis C virus; LR(−), negative likelihood ratio; LR(+), positive likelihood ratio; NPV, negative predictive value; POC, point of care; . PPV, positive predictive value; SA, (manufacturer's) screening assay.

Recent and ongoing studies

One ongoing or in-development trial of the OraQuick HCV for identification of anti-HCV antibodies was identified in the preparation of this briefing.

- NCT02084719: Comparison of OraQuick HCV Rapid Antibody Test and Standard Serologic Screening for Hepatitis C: Validity, Acceptability and Impact on Linkage to Care. Status: currently recruiting.

Costs and resource consequences

No published evidence relating to cost or resource consequences of using the OraQuick HCV in the NHS was identified for this briefing.

In order to begin using the OraQuick HCV in a primary care, community clinic or hospital setting, no additional apparatus or training would be needed. The test may save staff time because a result can be read in 20 minutes and in a single appointment. Current standard practice requires blood samples be sent to a laboratory for enzyme immunoassay testing, which can take around a week. Some patients do not return for a second appointment, so staff time is used trying to contact patients; this is particularly pressing for patients with positive antibody test results. A rapid, point-of-care test such as the OraQuick HCV could minimise staff time used in this way.

Strengths and limitations of the evidence

The published evidence is limited to cohort/cross-sectional diagnostic studies; no randomised controlled trials were identified. Of the identified studies, Drobnik et al. (2011), Gao et al. (2014), Hayes et al. (2014) and Larrat et al. (2012) had consecutive recruitment. Cha et al. (2014), Lee et al. (2010), Lee et al. (2011), Morano et al. (2014), Scalioni et al. (2014) and Smith et al. (2011) did not state whether the patients were randomised or consecutively recruited. There is a risk of selection bias in non-consecutive studies.

Some of the studies identified enrolled people whose HCV status was unknown, which is a more realistic reflection of clinical practice. These were: Drobnik et al. (2011), Gao et al. (2014), Hayes et al. (2014), Lee et al. (2011), Morano et al. (2014), Scalioni et al. (2014) and Smith et al. (2011).

Only the study by Gao et al. (2014) states that testers were blinded as to the patient's HCV status and if they were performing a re-test. Blinding minimises any bias introduced by researchers and clinical staff administering the tests. The study by Lee et al. (2011) specifically states that samples were tested in an unblinded fashion. None of the other studies stated whether the tests were blinded or not.

The studies by Cha et al. (2014), Larrat et al. (2012) and Lee et al. (2010) enrolled people knowing their HCV-status. It is not clear whether any of the researchers were blinded to patients' HCV status.

The studies by O'Connell et al. (2013) and Cha et al. (2014) tested blood samples from blood banks or commercial sources, where HCV status was known. This is a limitation because samples were not taken from a patient in a real-life clinical setting. It is not clear whether any of the researchers were blinded to the HCV status of the blood samples.

Drobnik et al. (2011), Morano et al. (2014), Scalioni et al. (2014) and Smith et al. (2011) used community or mobile unit testing as a setting for the OraQuick HCV.

Only Morano et al. (2014) reported linking patients to specialised hepatitis care following diagnosis.

There were 3 studies that were funded by the manufacturer of the OraQuick HCV (OraSure), or for which OraSure staff are listed as authors:

- Drobnik et al. (2011) (funded by OraSure)
- Lee et al. (2010) (funded by OraSure and Lee was employed by OraSure)
- Lee et al. (2011) (Lee was employed by OraSure).

Relevance to NICE guidance programmes

The use of the OraQuick HCV is not currently planned into any NICE guidance programme.

NICE has issued the following guidance relevant to this briefing:

- Hepatitis B and C: ways to promote and offer testing to people at increased risk of infection (2012) NICE public health guidance 43
- Peginterferon alfa and ribavirin for the treatment of chronic hepatitis C (2010) NICE technology appraisal guidance 200
- Interferon alfa (pegylated and non-pegylated) and ribavirin for the treatment of chronic hepatitis C (2004) NICE technology appraisal guidance 75
- Peginterferon alfa and ribavirin for the treatment of mild chronic hepatitis C (2006) NICE technology appraisal guidance 106
- Peginterferon alfa and ribavirin for treating chronic hepatitis C in children and young people (2013) NICE technology appraisal guidance 300
- Telaprevir for the treatment of genotype 1 chronic hepatitis C (2012) NICE technology appraisal guidance 252
- Boceprevir for the treatment of genotype 1 chronic hepatitis C (2012) NICE technology appraisal guidance 253

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Search strategy and evidence selection

Search strategy

A strategy was designed in Medline and adapted for the following databases:

- Medline In Process
- Embase
- Cochrane library (CDSR, CENTRAL, DARE, HTA, NHS EED and HEED).

Additional searches were also conducted of the following:

- ClinicalTrials.gov
- ICTRP
- FDA MAUDE
- MHRA.

Evidence selection

References were imported into Reference Manager and screened independently in duplicate by title and abstract. The full publications, where available, of selected references were also screened independently in duplicate. Data from each of the studies were extracted by 1 reviewer and independently checked for accuracy by a second reviewer. Disagreements were resolved through discussion. Studies were assessed for quality by using an adapted version of the QUADAS-2 tool as directed by the NICE interim process and methods statement. Assessment was performed by 1 reviewer and independently checked by a second reviewer and disagreements resolved by discussion.

Three studies were excluded:

- Villar et al. 2012 is a poster abstract. It may also contain some patient data that crosses over with the Scalioni et al. 2014 study.
- Lee et al. 2012 is a conference abstract only, and therefore does not contain much

methodological detail.

- Stockman et al. 2014 is a screening study using OraQuick in four HCV community outreach sites in Wisconsin, USA. Only positive OraQuick samples had follow-up EIA and PCR tests, and therefore no diagnostic performance data could be calculated for OraQuick from the results.

About this briefing

Medtech innovation briefings summarise the published evidence and information available for individual medical technologies. The briefings provide information to aid local decision-making by clinicians, managers, and procurement professionals.

Medtech innovation briefings aim to present information and critically review the strengths and weaknesses of the relevant evidence, but contain no recommendations and are not formal NICE guidance.

Development of this briefing

This briefing was developed for NICE by Cedar. The interim process and methods statement sets out the process NICE uses to select topics, and how the briefings are developed, quality assured and approved for publication.

Project team

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The following specialist commentators provided comments on a draft of this briefing:

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ISBN: 978-1-4731-1053-3