
Elephant

World Health Organization

UPDATED RECOMMENDATIONS ON

SIMPLIFIED SERVICE DELIVERY AND DIAGNOSTICS FOR HEPATITIS C INFECTION

POLICY BRIEF

Updated recommendations on simplified service delivery and disagnostics for hepititis C infection: policy brief

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ACRONYMS AND ABBREVIATIONS

ART	antiretroviral treatment
DBS	dried blood spot
EID	early infant diagnosis
EQA	external quality assessment
GDG	Guidelines Development Group
GRADE	Grading of Recommendations Assessment, Development and Evaluation
GRC	Guidelines Review Committee
HCV	hepatitis C virus
HIV	human immunodeficiency virus
IQC	internal quality control
LMIC	low- and middle-income countries
LoD	limit of detection
NAT	nucleic acid testing
NSP	needle and syringe programme
OAMT	opioid agonist maintenance therapy
POC	point-of-care
RCT	randomized controlled trial
RDT	rapid diagnostic test
RNA	ribonucleic acid
SVR	sustained virological response
STI	sexually transmitted infection
TAT	turn-around time
TB	tuberculosis
WHO	World Health Organization

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GUIDELINES DEVELOPMENT GROUP

Co-chairs: Anchalee Avihingsanon (HIV-NAT, Thai Red Cross AIDS Research Centre, Bangkok, Thailand) and Saeed Sadiq Hamid (The Aga Khan University, Pakistan). GRADE methodologist: Roger Chou (Oregon Health and Science University, Portland, United States of America (USA)).

Muhammad Radzi Abu Hassan (Ministry of Health, Malaysia), Suna Balkan (Médecins Sans Frontières, France), Ajeet Singh Bhadoria (All India Institute of Medical Sciences, Rishikesh, India), Judy Chang (International Network of People Who Use Drugs, United Kingdom of Great Britain and Northern Ireland), Nikoloz Chkhartishvili (Infectious Diseases, AIDS and Clinical Immunology Research Centre, Georgia), Vladimir Chulanov (National Medical Research Centre for TB and Infectious Diseases, Russian Federation), Geoffrey Dusheiko (King's College Hospital, United Kingdom), Manal Hamdy El-Sayed (Ain Shams University, Egypt), Maria Butí (Hospital Universitario Valle Hebron, Spain), Jason Grebely (Kirby Institute, University of New South Wales (UNSW), Sydney, Australia), Cary James (World Hepatitis Alliance, United Kingdom), Saleem Kamili (Centers for Disease Control and Prevention, United States of America), Ibtissam Khoudri (Ministry of Health, Morocco), Giten Khwairakpam (TREAT Asia, Thailand), Tammy Meyers (School of Women's and Children's Health, UNSW, Sydney, Australia), Christian B. Ramers (Clinton Health Access Initiative, USA), Cielo Yaneth Ríos-Hincapié (Ministry of Health and Social Protection, Colombia), Janvier Serumondo (Rwanda Biomedical Centre, Rwanda), Mark Sonderup (University of Cape Town, South Africa), Lai Wei (Beijing Tsinghua Changgung Hospital, Tsinghua University, Beijing, China), Ernst Wisse (Médecins du Monde, France).

WHO STEERING COMMITTEE

WHO headquarters staff: Philippa Easterbrook, Emmanuel Fajardo, Asma Hafiz, Olufunmilayo Lesi, Niklas Luhmann, Robert Luo, Martina Penazzato, Anita Sands, Lara Vojnov (Global HIV, Hepatitis and Sexually Transmitted Infection Programme).

WHO regional office staff: Po-Lin Chan (Regional Office for the Western Pacific), Casimir Mingiedi Mazengo (Regional Office for Africa), Bridget Mugisa (Regional Office for the Eastern Mediterranean), Antons Mozalevskis (Regional Office for Europe), Bharat Bhushan Rewari (Regional Office for South-East Asia), Leandro Soares Sereno (Pan American Health Organization).

OVERALL COORDINATION AND WRITING

Philippa Easterbrook (Global HIV, Hepatitis and Sexually Transmitted Infection Programme, WHO Headquarters, Switzerland). Support was provided by Marcelo Contardo Moscoso Naveira and also by Diana Faini (WHO Headquarters).

BACKGROUND

Hepatitis C virus (HCV) infection is a major public health problem and cause of chronic liver disease that leads to approximately 400 000 deaths annually. In 2019 WHO estimated that 58 million persons were chronically infected and living with hepatitis C, with a disproportionately high burden in low- and middle-income countries (LMICs). In 2016 WHO developed the Global Health Sector Strategy on viral hepatitis 2016–2021, with the ambitious goal to eliminate viral hepatitis as a public health threat by 2030. While good progress has been made in several champion countries, there remains a major testing and treatment gap. In 2019, still only 21% of the 58 million persons with chronic HCV infection had been diagnosed, and 13% treated *(1)*. Achieving the 2030 90% testing and 80% treatment coverage targets for HCV elimination will require a radical simplification of care pathways to overcome barriers in access to HCV testing and treatment.

Reaching the 2030 90% testing and 80% treatment coverage targets for HCV elimination will require a substantial simplification of service delivery.

OVERVIEW OF UPDATED HCV GUIDELINES

The WHO 2022 HCV guidelines, *Updated recommendations on treatment of children and adolescents and children with chronic HCV infection, and HCV simplified service delivery and HCV diagnostics (1)* provide updated, evidence-based recommendations on priority HCV-related topics where there is key new evidence and other supporting data. It builds upon the *2018 WHO Guidelines for the care and treatment of persons diagnosed with chronic hepatitis C virus infection (2)* and the *2017 WHO Guidelines on hepatitis B and C testing (3)*.

The three main areas of new recommendations are:

- **Simplified service delivery (decentralization, integration and task sharing):** Expansion of HCV testing and treatment services, ideally at the same site, through decentralization of care to lower-level facilities; integration with existing services, such as in primary care, harm reduction programmes, prisons and HIV services; and promotion of task sharing through delivery of HCV testing, care and treatment by appropriately trained non-specialist doctors and nurses.
- **HCV diagnostics – use of Point-of-care (POC) HCV RNA viral load and reflex HCV RNA viral load testing:** The use of point-of-care (POC) HCV ribonucleic acid (RNA) assays is now recommended as an alternative approach to laboratory-based RNA assays to diagnose viraemic infection. This is especially applicable to marginalized populations, such as persons who inject drugs, and hard-to-reach communities with limited access to health care and high rates of loss to follow-up.

  Reflex HCV RNA testing in those with a positive HCV antibody test is recommended as an additional strategy to promote linkage to care and treatment. This can be achieved either through laboratory-based reflex HCV RNA testing following a positive HCV antibody test, using a specimen already held in the laboratory,

or clinic-based reflex testing in a health facility through immediate specimen collection for HCV RNA testing following a positive rapid HCV antibody test. Both these approaches avoid the need for an additional clinic visit.

- **Use of direct-acting antiviral (DAA) treatment of adolescents and children ages ≥3 years[1]:** New treatment recommendations extend the 2018 "treat all" recommendation for adults with chronic HCV infection to include adolescents and children down to 3 years. They also align existing recommended DAA regimens for adults (sofosbuvir/daclatasvir (SOF/DCV), sofosbuvir/velpatasvir (SOF/VEL) and glecaprevir/pibrentasvir (G/P)) to use in adolescents and children. This alignment is expected to simplify procurement, promote access to treatment among children in LMICs and contribute to global efforts to eliminate the disease[1].

[1] WHO Updated recommendations on treatment of adolescents and children with chronic HCV infection. Policy Brief. Geneva: World Health Organization; 2022

These guidelines also include updates to existing chapters without new recommendations, such as inclusion of new manufacturers' protocols on use of dried blood sport (DBS) specimens for HCV serology and RNA viral load testing, and new data to inform limit of detection (LoD) for HCV RNA viral load assays as a test of cure.

This policy brief, one of two on the updated HCV guidelines, focuses on the new recommendations on simplified service delivery for a public health approach to HCV testing, care and treatment. These recommendations include decentralization, integration and task-sharing, in addition to the use of POC HCV viral load assays and reflex viral load testing. In 2023 all updated recommendations for hepatitis B and C will be collated along with existing recommendations into a single consolidated guidelines on prevention, testing, care and treatment of hepatitis B and C, containing all relevant guidance on viral hepatitis.

Intended audience

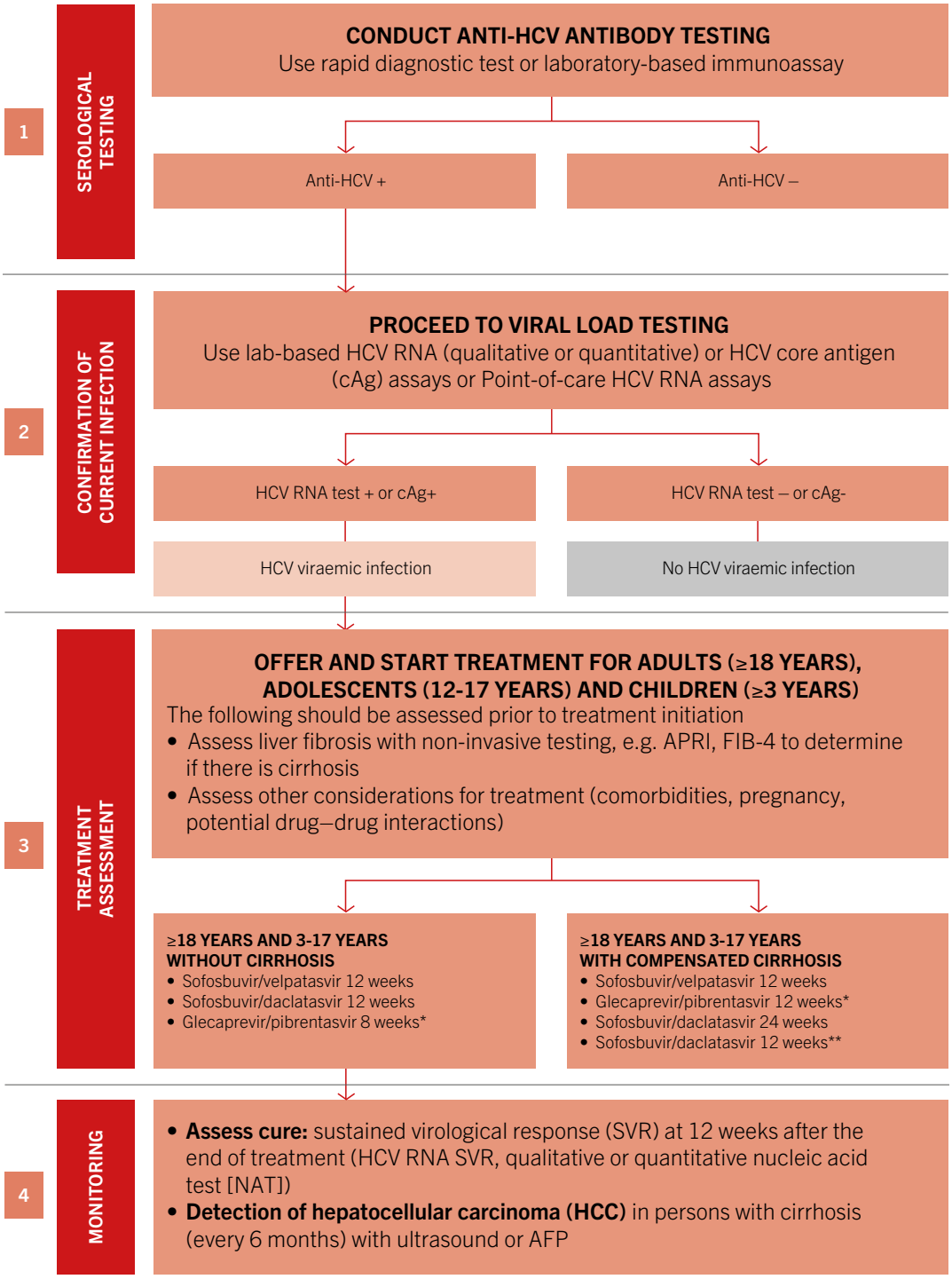
These guidelines are primarily addressed to national hepatitis programme managers and other policymakers in ministries of health, particularly in LMICs, who are responsible for the development of national hepatitis testing and treatment policies and guidelines. These guidelines will also be useful for laboratory managers in reference and key hospital laboratories who are responsible for development of national testing algorithms, and procurement of assays, quality control (QC) and quality assurance (QA). Finally, the guidelines will serve as a reference for health care providers who offer and implement hepatitis testing, care and treatment for persons with hepatitis C virus infection, including those working in community-based programmes.

Guidelines methodology

In accordance with the procedures established by the WHO Guidelines Review Committee (GRC), a regionally representative and multidisciplinary Guidelines Development Group (GDG) met in October 2021 to formulate the recommendations using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach *(4)*. Evidence to inform the recommendations included four commissioned systematic reviews and meta-analyses, an assessment of the overall balance of benefits and harms (at individual and population levels), community and health worker values and preferences, resource use, cost–effectiveness, considerations on equity and human rights, and feasibility across the different WHO regions.

FIGURE 1

Summary algorithm for the diagnosis, treatment and monitoring of chronic HCV infection in adults, adolescents and children ≥ 3 years



* Persons with HCV genotype 3 infection who have received interferon and/or ribavirin in the past should be treated for 16 weeks.

** May be considered in countries where genotype distribution is known and genotype 3 prevalence is <5%.

SUMMARY OF 2022 RECOMMENDATIONS FOR SIMPLIFIED SERVICE DELIVERY AND HCV DIAGNOSTICS

The following table presents the recommendations, including the strength of the recommendation and certainty of evidence, on simplified service delivery, POC HCV RNA testing, and reflex HCV RNA viral load testing.

Recommendation	Existing, updated or new recommendation
Simplified service delivery	
Decentralization:[1] We recommend delivery of HCV testing and treatment at peripheral health or community-based facilities, and ideally at the same site, to increase access to diagnosis, care and treatment. These **facilities** may include primary care, harm reduction sites, prisons and HIV/ART clinics as well as community-based organizations and outreach services. *(strong recommendation; certainty of evidence:[2] moderate (people who inject drugs, prisoners); low (general population, people living with HIV)*	New
Integration:[3] We recommend integration of HCV testing and treatment with existing care services at peripheral health facilities. These **services** may include primary care, harm reduction (needle and syringe programme (NSP)/opioid agonist maintenance therapy (OAMT) sites), prisons and HIV/ART services. *(strong recommendation; certainty of evidence: moderate (people who inject drugs, prisoners); low (general population, people living with HIV))*	New
Task sharing:[4] We recommend delivery of HCV testing, care and treatment by trained non-specialist doctors and nurses to expand access to diagnosis, care and treatment. *(strong recommendation; moderate certainty of evidence)*	New

[1] Decentralization of services refers to service delivery at peripheral health facilities, community-based venues and locations beyond hospital sites or conventional health care settings, bringing care nearer to patients' homes.

[2] The systematic review was based on an analysis by population group (people who inject drugs, prisoners, general population and people living with HIV) rather than setting or services (harm reduction sites, prisons, primary care or HIV/ART clinics), although these were highly related to population group.

[3] Integrated service delivery refers to delivery of different health services in a way that ensures people receive a continuum of health promotion, disease prevention, diagnosis and treatment.

[4] Task-sharing refers to the rational redistribution of tasks from "higher-level" cadres of health care providers to other cadres, such as trained lay providers, including community members.

HCV RNA testing – Detection of viraemic HCV infection	
Laboratory-based HCV NAT testing: Directly following a positive HCV antibody serological test result, the use of quantitative or qualitative nucleic acid testing (NAT) for detection of HCV ribonucleic acid (RNA) is recommended as the preferred strategy to diagnose viraemic infection. *(strong recommendation; moderate/low certainty of evidence)*	Existing[1]
HCV core antigen assay: An assay to detect HCV core (p22) antigen, which has comparable clinical sensitivity to laboratory-based HCV RNA NAT assays, can be an alternative approach to diagnose HCV viraemic infection. *(conditional recommendation, moderate certainty of evidence)*	Existing[1]
Point-of-care (POC) HCV RNA assays: The use of HCV point-of-care (POC) viral load NAT assay can be an alternative approach to laboratory-based HCV RNA NAT assays to diagnose HCV viraemic infection. *(conditional recommendation; low/moderate certainty of evidence)*	New
HCV RNA testing – Assessment of treatment response	
Laboratory-based HCV RNA NAT assays: Nucleic acid testing (NAT) for qualitative or quantitative detection of HCV RNA should be used as test to document cure at 12 or 24 weeks (that is, sustained virological response (SVR12 or SVR24)) after completion of antiviral treatment. *(conditional recommendation; moderate/low certainty of evidence)*	Existing[1]
Point-of-case HCV RNA assays: Point-of-care (POC) HCV RNA assays with comparable limit of detection to laboratory-based assays can be used as an alternative approach as test of cure. *(conditional recommendation; low/moderate certainty of evidence)*	New
Reflex HCV RNA viral load testing	
We recommend reflex HCV RNA testing in those with a positive HCV antibody test result as an additional key strategy to promote linkage to care and treatment. This can be achieved either through **laboratory-based reflex HCV RNA** testing following a positive HCV antibody test using a specimen already held in the laboratory, or **clinic-based reflex testing** in a health facility through immediate specimen collection following a positive HCV antibody RDT.[2] *(conditional recommendation; low certainty of evidence)*	New

[1] WHO Guidelines on hepatitis B and C testing. Geneva WHO 2018

[2] Reflex testing is a linked HCV RNA (or HCVAg) test that is triggered among all people who have an initial positive HCV antibody screening test result. Reflex HCV RNA testing may be implemented in two ways: either laboratory-based reflex testing or clinic-based reflex testing.

SIMPLIFIED SERVICE DELIVERY: DECENTRALIZATION AND INTEGRATION

Recommendation

Decentralization: We recommend delivery of HCV testing and treatment at peripheral health or community-based facilities, and ideally at the same site, to increase access to diagnosis, care and treatment. These **facilities** may include primary care, harm reduction sites, prisons and HIV/ART clinics as well as community-based organizations and outreach services.

(strong recommendation; certainty of evidence:[1] *moderate (people who inject drugs/prisoners); low (general population/people living with HIV))*

Integration: We recommend integration of HCV testing and treatment with existing care services at peripheral health facilities. These **services** may include primary care, harm reduction (NSP/OAMT), prison health and HIV/ART services.

(strong recommendation; certainty of evidence: moderate (people who inject drugs/prisoners); low (general population/people living with HIV))

Background

In the 2018 update to the WHO HCV guidelines *(2)*, WHO described eight key good practice principles to simplify service delivery across the continuum of care and to support implementation of the "Treat All" recommendations **(Box 1)**. There is now substantial evidence for three of these key interrelated components of HCV simplified service delivery to support new WHO recommendations – decentralization of services away from specialized centres; integration of hepatitis testing, care and treatment with other existing services; and task sharing to non-specialist health care workers.

The overall goal is to expand the reach and uptake of viral hepatitis care by facilitating access to hepatitis testing and treatment alongside other health services, while making hepatitis B and C testing and treatment more convenient for people coming to health facilities. WHO already recommends integration of HIV testing into a range of other clinical services, such as services for tuberculosis (TB), HIV/ART, maternal and child health, screening for noncommunicable diseases, sexual and reproductive health (especially sexually transmitted infection (STI) clinics), mental health, harm reduction programmes, migrant and refugee services and in prisons *(6)*. Given the shorter duration and simplicity of HCV treatment, there are even greater opportunities for decentralization, integration and task sharing of HCV testing and treatment.

[1] The systematic review was based on an analysis stratfied by population group (people who inject drugs, prisoners, general population and people living with HIV) rather than setting or services (harm reduction sites, prisons, primary care or HIV/ART clinics), although these were highly related to population group.

Key definitions

Decentralization of services refers to delivery at peripheral health facilities, community-based venues and locations beyond hospital service sites, bringing care nearer to patients' homes.

Integrated service delivery refers to delivery of different health services in a way that ensures that people receive a continuum of health promotion, disease prevention, diagnosis and treatment.

Task sharing involves the strategic redistribution of tasks among health workforce teams and personnel. Specific tasks are moved, shared and delegated, usually from highly trained health workers to those with shorter training or fewer qualifications.

BOX 1. Good practice principles for HCV health service delivery, from the 2018 Guidelines for the care and treatment of persons diagnosed with chronic hepatitis C virus infection *(2)*

1. Comprehensive national planning for the elimination of HCV infection based on local epidemiological context; existing health care infrastructure; current coverage of testing, treatment and prevention; and available financial and human resources.
2. Simple and standardized algorithms across the continuum of care from testing through linkage to care and treatment.
3. Strategies to strengthen linkage from testing to care, treatment and prevention.
4. Integration of hepatitis testing, care and treatment with other services to increase the efficiency and reach of hepatitis services. **New recommendation**
5. Decentralized testing and treatment services at primary health facilities or harm reduction sites to promote access to care. **New recommendation**
6. Task sharing, supported by training and mentoring of health care workers and peer workers. **New recommendation**
7. Differentiated care strategy to assess needs at different levels of carte, with specialist referral as appropriate for those with complex problems.
8. Community engagement and peer support to promote access to services and linkage through the continuum of care, which includes addressing stigma and discrimination.
9. Strategies for more efficient procurement and supply management of quality-assured, affordable medicines and diagnostics.
10. Data systems to monitor the quality of individual care and coverage at key steps along the continuum, or cascade, of care at the population level.

Summary of the evidence

A WHO-commissioned systematic review and meta-analysis of 142 studies from 33 countries (20 studies (14%) were in LMICs) examined the effectiveness of key simplified service delivery interventions – decentralization, integration and task sharing to non-specialists – in terms of outcomes across the HCV cascade of care *(6)*. Eighty studies (56%) were conducted among people who inject drugs; 20 (14%) were among people in prisons; five (4%) in people living with HIV; and 37 (26%) in the general population. Of the 142 studies, 123 studies (87%) were single-arm, and 11 (8%) were comparator observational studies. There were only six randomized controlled trials (RCTs).

Among people who inject drugs, there was higher HCV RNA testing uptake with full decentralization/integration (98% [95% CI: 95–100%]) at harm reduction sites than with partial decentralization (81% [95% CI: 69–91%]) or no decentralization (82% [95% CI:13–100%]). DAA treatment uptake levels also were higher with full decentralization/integration (73% (95% CI: 63–80%) compared with partial decentralization (66% [95% CI: 55–77%]) and no decentralization (35% [95% CI: 23–48%]).

Similarly, **for those in prison settings,** there was higher linkage to care with full decentralization and integration into existing prison services than with partial decentralization: 94% (95% CI:79–100%) versus 50% (95% CI: 29–71%) as well as higher DAA treatment uptake: 72% (95% CI: 48–91%) versus 39% (95% CI: 17–73%).

For general populations, with decentralization and integration of HCV testing and treatment into primary care services, there was a high degree of heterogeneity for all outcomes.

The proportion of patients achieving cure (SVR12) was high (>95%) across all levels of decentralization/integration and for all populations. The findings among people who inject drugs were confirmed in studies with comparator arms, which found higher linkage to care with full decentralization/integration of HCV testing at harm reduction sites than with no decentralization/integration: 88% (95% CI: 77–94%) versus 67% (95% CI: 54–78%) (P=0.008) and higher uptake of treatment: 88% (65–100%) versus 33% (25–43%) (P<0.001).

Supporting evidence from HIV literature for decentralization and integrated care

Additional indirect evidence to inform simplified approaches to HCV care and diagnosis, such as decentralization of care to lower level health facilities and task sharing with nurses and non-specialists, comes from the HIV literature *(7)*. Decentralization was a key factor in the successful global scale-up of HIV treatment services, improving uptake of both testing and treatment and reducing loss to follow-up *(8, 9)*.

Rationale for recommendations

The Guideline Development Group (GDG) made a strong recommendation to adopt fully decentralized HCV testing and treatment at the same peripheral health care facility and full integration of HCV testing and treatment services into existing primary care, harm reduction services, prisons and HIV clinics. This recommendation was based on evidence of moderate certainty of increased uptake of HCV viral load testing, linkage to care and treatment at harm reduction sites among people who inject drugs, as well as among prisoners in closed settings, and evidence of low certainty among the general population in primary care settings.

Criteria	Rationale for recommendation
Overall balance of benefits and harms	1. Decentralization of HCV testing and treatment to lower-level facilities will increase access to HCV testing and treatment services and so accelerate progress towards elimination. 2. Delivery of HCV testing, care and treatment nearer to the patient, ideally as a "one-stop-shop", is more convenient for patients, requiring fewer visits. 3. Co-location and integration of HCV testing and treatment services with existing harm reduction or primary care services facilitates meeting multiple needs in one easily accessible setting. 4. For the health system, integration of HCV testing and care into existing primary care or harm reduction services may reduce duplication of services and improve coordination (for example, in stock management of diagnostic assays) The key challenges with decentralization are that there is usually less specialist expertise at decentralized sites, and a good triage system is needed to ensure that those in need of more specialist care are identified and referred. Overall, the GDG considered that the benefits substantially outweighed any potential harms.
Cost and cost–effectiveness	Four studies have evaluated the cost–effectiveness of different levels of decentralization and task sharing *(10-13)*. All support the cost-effectiveness of simplified care models.
Acceptability, values and preferences	Three related surveys and a series of in-depth interviews were undertaken among different populations affected by HCV to inform an understanding of the acceptability of different ways of simplifying delivery of care. Overall, there was strong support for fully decentralized and integrated HCV services offering testing and treatment at the same community site and near to people's homes rather than in hospitals. The importance of a non-judgmental/non-stigmatizing approach among health care providers was also highlighted, especially by those who inject drugs or living with HIV.
Equity	The evidence review showed that the impact of full decentralization/integration of HCV testing and treatment was greatest among people who inject drugs and prisoners – two marginalized populations that have particular difficulties accessing health services and have high rates of loss to follow-up.
Feasibility	Decentralization was a key factor in successful global scale-up of HIV treatment services, improving uptake of both testing and treatment and reducing loss to follow-up. There are now multiple examples of successful models of decentralized viral hepatitis C testing and treatment services emerging in high-burden countries, both in primary care for the general population and at harm reduction sites for people who inject drugs.

Implementation considerations

Implementation of the recommendations should be informed by local context, including HCV epidemiology and the prevalence of comorbidities, the availability of resources, the organization and capacity of the health system and anticipated cost–effectiveness.

- **Decentralization and/or integration.** These approaches to simplifying HCV testing and treatment services will require additional training and supervision for health care workers (see Task-sharing Implementation considerations, page 19), access to quality-assured RDTs or collection and analysis of dried blood spot (DBS) specimens, good specimen referral networks and documentation of results, including other features such as enhanced connectivity for return of results and an electronic results reporting system. Planning and coordination are also important for delivery of integrated care, including establishment of integrated data systems and consistent cross-training of health care providers.
- **Implementation alongside other existing good practice principles of simplified service delivery** (see Box 1). These include comprehensive national planning, simple and standardized algorithms, differentiated care strategy, community engagement and peer support, more efficient procurement and supply management and data systems to monitor coverage and the quality of individual care.
- **Adaptation of service delivery recommendations for different contexts, including high-income countries.**
  - **Decentralization of HCV testing and treatment services may not be appropriate for all settings or acceptable to all clients.** The relative benefits and costs should be assessed according to the context. For example, decentralization of services may be inefficient and costly in high-income countries with a low burden of HCV infection, where a centralized service delivery model with community linkage may be more appropriate.
  - **Adaptations may be needed for specific populations.** Although hepatitis care and treatment services for key populations can be provided in decentralized settings, it should be recognized that not all health care centres are equally able to deal with the specialized needs of people who use drugs. The experience of stigma and discrimination is one of the major problems in accessing services for people who inject drugs, and this problem may be greater at some facilities than others. Some may choose to receive their hepatitis care in a facility that is not close to their homes because of concerns about stigma and disclosure.

SIMPLIFIED SERVICE DELIVERY: TASK SHARING

Recommendation: Task sharing

We recommend delivery of HCV testing, care and treatment by trained non-specialist doctors and nurses to expand access to diagnosis, care and treatment.

(strong recommendation; moderate certainty of evidence)

Background

Until recently, delivery of hepatitis C testing and treatment in many countries relied on specialist-led (usually by a hepatologist or gastroenterologist) centralized care models in hospital settings to administer complex treatment. The advent of short-course oral, curative pangenotypic HCV DAA treatment regimens with few if any side-effects means that minimal expertise and monitoring are now required. HCV care, therefore, has the potential to be safely provided by non-specialists, including primary care physicians and nurses at peripheral or community facilities. Task sharing to non-specialists is also a pragmatic response to shortages of highly trained health workers and specialists in the management of viral hepatitis. In 2014, WHO strongly recommended task sharing for HIV care, based on a comprehensive evidence base, and this has been widely adopted to expand access to HIV testing and ART initiation and follow-up *(14, 15)*. There is now also a substantial evidence base on sharing HCV care tasks to non-specialist health care workers to inform updated WHO recommendations.

Summary of the evidence

A systematic review and meta-analysis of 142 studies from 33 countries (20 (14%) from LMICs) examined the effectiveness of task sharing to non-specialists, alongside the other simplified service delivery interventions of decentralization and integration, on outcomes across the HCV cascade of care. There were 46 (30%) studies of care delivered by non-specialists; 24 (16%) studies of care delivered by non-specialists supported through telehealth; and 51 (33%) assessed care delivered by specialists. Of the 142 studies, 80 (56%) were among people who inject drugs, 20 (14%) among people in prisons, five (4%) in people living with HIV and 37 (26%) in the general population.

Across all populations and settings, task sharing of care and treatment with DAA-based regimens to a non-specialist (primary care physician, addiction specialist or nurse) was associated with consistently high SVR12 cure rates, similar to rates among those who received treatment by specialists. This included among people who inject drugs (non-specialists, 96% [95% CI: 93–98%] compared with specialists, 92% [95% CI: 88–96%]); people in prisons (non-specialists, 98% [95% CI: 96–99%] compared with specialists, 100% [95% CI: 77–100%]), people living with HIV (non-specialists, 98% [95% CI: 96–99] compared with specialists, 100% [95% CI: 96–100], and the general population (non-specialists 94% [90–97] compared with specialists 94% [92–96]).

Additional supporting evidence from the HIV literature

Multiple systematic reviews from different areas of health care demonstrate that good health outcomes can be achieved by devolving tasks to nurses and lay or community health workers with appropriate training and supervision *(16, 17)*. Task sharing has been adopted for around two decades to expand HIV testing and treatment across the globe, especially in resource-limited settings where there is a shortage of health care professionals *(18, 19)*.

Rationale for recommendations

The Guideline Development Group made a strong recommendation for adoption of task sharing in HCV care to non-specialists, including primary care physicians and nurses, based on moderate certainty of evidence of comparable cure rates between specialists and non-specialists across all populations and in all settings.

Criteria	Rationale for recommendation
Overall balance of benefits and harms	• Task sharing is a key intervention to improve access to HCV diagnosis and treatment, especially among people who inject drugs and people in prisons, who are more challenging populations to reach and treat. • Multiple systematic reviews from different areas of health care demonstrate that good health outcomes can be achieved by devolving tasks to nurses and lay or community health workers with appropriate training and supervision *(16, 17)*. • Task sharing has been adopted for around two decades to expand HIV testing and treatment across the globe, especially in resource-limited settings where there is a shortage of health care professionals. • There is little reported evidence of harms with task sharing in HCV service delivery, but adequate training and support is required to ensure referral for more complex cases.
Resource considerations and access	Four studies have evaluated the cost–effectiveness of different levels of decentralization and task sharing *(10-13)*. The simplified care models with task sharing to nurses or non-specialist doctors resulted in lower costs and either similar or better SVR12 cure rates and were considered very cost–effective.
Acceptability, values and preferences	Across three different surveys undertaken to understand the acceptability of task sharing of HCV services to different populations affected by HCV, respondents recognized that non-specialists (primary care physicians, nurses, community health workers, pharmacists) already play important roles in HCV testing and treatment and that this can help promote testing uptake and linkage to care. Also, there was unanimous support for the critical importance of a non-judgmental/non-stigmatizing approach among health care providers and this needs to be addressed in training. There was strong support for additional peer-based and community-led HIV/STI/HCV services.
Equity	The evidence review showed that the impact of decentralisation and task-shifting was greatest among people who inject drugs and prisoners – two marginalized populations that have particular difficulties accessing health services. Surveys of end-users suggest that delivery of HCV testing and treatment by staff at harm reduction sites is associated with less stigma and, as a result, promotes access.
Feasibility	Many studies and programmes show the feasibility of task sharing of HCV diagnosis and treatment to non-specialists in primary care and among the marginalized people who inject drugs at OAMT and NSP sites.

Implementation considerations

- **Training and mentorship.** Effective task sharing with non-specialist doctors or nurses requires appropriate training and ongoing mentorship at the decentralized site and access to additional support or referral to tertiary or specialist sites for more complex cases. This should include awareness-raising and training to ensure provision of non-stigmatizing, non-discriminatory health care to key populations.
- **Defining roles and standards of care:** Standards of care should be defined for different levels of the health system, including the private sector. The role of each cadre of health worker should match their skills and capacity, and the lines of responsibility should be clear and well understood. There is a need to ensure an appropriate mix of health care workers at peripheral facilities.
- **Regulatory framework:** An appropriate regulatory framework (laws, regulations, policies and guidelines) is needed to enable tasks to be performed by different cadres of health care workers. In some countries task sharing and delegation may require changes to legislation and rules and procedures. It is not yet understood how task sharing for hepatitis C care could apply to children's care, due to the need to adjust the dosage for younger children.

HCV DIAGNOSTICS: USE OF POINT-OF-CARE (POC) HCV RNA ASSAYS FOR DETECTION OF HCV VIRAEMIC INFECTION TO GUIDE TREATMENT, AND AS TEST OF CURE

Existing and new recommendations: Detection of HCV viraemic infection

Existing recommendations from 2017 WHO Guidelines on hepatitis B and C testing *(3)*:

Laboratory-based HCV NAT assays: Directly following a positive HCV antibody serological test result, the use of quantitative or qualitative nucleic acid testing (NAT) for detection of HCV ribonucleic acid (RNA) is recommended as the preferred strategy to diagnose viraemic infection

(strong recommendation; moderate/low certainty of evidence).

HCV core antigen assays: An assay to detect HCV core (p22) antigen, which has comparable clinical sensitivity to laboratory-based HCV RNA NAT assays, can be an alternative approach to diagnose HCV viraemic infection[1]

(conditional recommendation; moderate certainty of evidence).

New 2022 recommendation:

POC HCV RNA assays: The use of HCV point-of-care (POC) viral load NAT assay can be an alternative approach to laboratory-based HCV RNA NAT assays to diagnose HCV viraemic infection

(conditional recommendation; low/moderate certainty of evidence).

Existing and new recommendations: Assessment of HCV treatment response – Test of cure

Existing recommendation from 2017 WHO Guidelines on hepatitis B and C testing *(3)*:

Laboratory-based HCV NAT testing: Nucleic acid testing (NAT) for qualitative or quantitative detection of HCV RNA should be used as test of cure at 12 or 24 weeks (that is, sustained virological response (SVR12 or SVR24)) after completion of antiviral treatment

(conditional recommendation, moderate certainty of evidence).

New recommendation:

POC HCV RNA assays: Point-of-care (POC) HCV RNA assays with a comparable limit of detection to laboratory-based assays can be used as an alternative approach as a test of cure.

(conditional recommendation, low/moderate certainty of evidence).

[1] A lower level of analytical sensitivity can be considered if an assay is able to improve access (that is, an assay that can be used at the point of care or suitable for dried blood spot [DBS] specimens) and/or affordability. An assay with a limit of detection of 3000 IU/mL or lower would be acceptable and, based on available data, would identify 95% of those with viraemic infection.

Background

Diagnosis of viraemic HCV infection in those who are HCV antibody-positive distinguishes persons with viraemic HCV infection and in need of treatment from those who have cleared the infection. This diagnosis is generally made using laboratory-based NAT technologies (both quantitative and qualitative methods) to detect HCV RNA, but also using assays to detect HCV core (p22) antigen. Although NAT technologies are very sensitive and specific for the detection of viraemia, the high cost of these assays and laboratory requirements means that they are not readily available in resource-limited settings.

Assays to detect HCV RNA that may be used at or near the point of care (POC) and are potentially less costly are now commercially available. WHO has previously recommended use of POC molecular assays for the rapid first-step identification of rifampicin-resistant and multidrug-resistant TB and for routine diagnosis of TB. Since 2021, WHO now recommends POC assays for early HIV infant diagnosis and for HIV treatment monitoring *(18)*. WHO has prequalified one POC HCV RNA assay: the Xpert HCV Viral Load (Cepheid, USA) (an Xpert fingerstick assay is pending WHO PQ)[1] *(19-21)*.

Summary of the evidence

A systematic review and meta-analysis addressed the question of whether POC HCV RNA NAT testing increased the uptake of HCV RNA testing and HCV treatment initiation and reduced time to test results and treatment initiation compared with laboratory-based RNA assays. The review covered 45 studies comprising 27 364 persons (28 studies among people who inject drugs/homeless populations; four studies among prison populations; nine among general/mixed populations; and four among people living with HIV). All 45 were observational studies; there were no RCTs. Fourteen studies made direct within-study comparisons between a POC assay arm and a laboratory-based arm of HCV RNA assay.

Outcomes – turn-around time (TAT). The pooled median TAT between HCV antibody testing and treatment initiation was shorter with POC HCV RNA NAT assays on site (18.5 days [95% CI: 14–53]) than with either lab-based near-POC HCV RNA assays (64 days [95% CI: 64–64]) or lab-based high-throughput HCV RNA NAT assays (67 days [95% CI: 50–67]). This was mainly due to shorter TAT from HCV RNA testing to treatment initiation with POC assays.

Outcomes – HCV RNA testing uptake and treatment uptake. In studies that directly compared a POC HCV RNA NATA assay arm and a laboratory-based assay arm, the pooled relative risk for RNA viral load testing uptake (four studies) was 1.11 [95% CI: 0.89–1.38] and for treatment uptake (10 studies) was 1.32 [95% CI: 1.06–1.64], indicating better outcomes for POC assay arms.

Diagnostic accuracy. In a complementary systematic review and meta-analysis of the diagnostic performance (sensitivity and specificity) of POC HCV RNA assays compared with laboratory-based NAT (25 studies, n=8791), high sensitivity and specificity were observed across all study settings and populations in both LMICs and high-income countries and across different assays and specimen types. The pooled sensitivity was 99% [95% CI: 98–99%] and specificity was 99% [95% CI: 99–100%] compared with a lab-based reference standard.

Additional, supporting evidence from HIV and other diseases. In 2021 WHO recommended use of POC HIV RNA assays for early infant diagnosis of HIV and routine HIV viral load monitoring for people living with HIV on ART *(18)*. This recommendation was based on high certainty of evidence that the use of same-day POC assays for HIV early infant diagnosis (EID) reduces the time to diagnosis and initiation of treatment in infected infants and, used for HIV treatment monitoring, reduces the time to clinical action in persons on treatment with a detectable viral load *(18, 23)*.

Use of HCV POC RNA assays as test of cure. A multi-cohort analysis considered 5973 cases of detectable viraemia following HCV treatment in nine countries and two large clinical trial registries. Three countries, Egypt, the USA and Georgia, accounted for 80% of cases. There was a higher HCV viral load among cases from clinical trials than those from observational databases. In the former, 95% had an HCV RNA greater than 4030 IU/mL (95% CI: 24-4100) versus, in the latter, 214 IU/mL (95% CI: 166–266). In another analysis, involving 34 phase 2/3 clinical trials with 330 treatment failure patients (256), 97% had an HCV RNA level greater than 10 000 IU/mL 12 weeks post-treatment, and only 0.9% had a HCV RNA level less than 1000 IU/mL. The consensus is that the majority of persons with detectable viraemia at the SVR12 time point are above 1000 IU/mL. Therefore, technologies that can detect viral HCV RNA levels down to 1000 IU/mL would be sufficient for diagnosis of virological failure and clinical decision-making in the vast majority of individuals.

[1] https://unitaid.org/assets/HepC-Dx-Tech-Landscape_May2019.pdf and WHO PQ public reports, HCV: https://extranet.who.int/pqweb/vitro-diagnostics/prequalification-reports.

Rationale for recommendations

The Guidelines Development Group recognized that access to laboratory based NAT assays is limited in resource-limited settings and made a conditional recommendation to consider use of POC NAT assays as an alternative to lab-based NAT or core antigen assays to diagnose viraemic HCV infection, based on moderate-/low-quality evidence. The Guidelines Development Group also recommended the use of POC HCV NAT assays (in addition to existing either qualitative or quantitative laboratory-based assays) for detection of HCV RNA as a test of cure at 12 weeks after completion of treatment (or at 24 weeks if 12 weeks is not possible). All the WHO prequalified laboratory-based quantitative HCV PCR assays have an LoD under 20 IU/mL and the reviews showed technologies that can detect viral HCV RNA levels down to 1000 IU/mL identify majority of individuals with treatment failure.

Topic	Rationale for recommendation
Balance of benefits and harms	• POC HCV RNA NAT platforms can be used in lower levels of health facilities, given their relative ease of use and suitability for running a low volume of tests. These assays, therefore, offer an opportunity to confirm viraemia at or near where patient is receiving care. • POC HCV RNA assays can lead to greater uptake of and faster viral load testing and shorter time from testing to return of results to the clinician and treatment initiation. This is especially the case when used in fully decentralized care models, that is, where testing and treatment are available at the same site and potentially on the same day. Where patients need to travel to another site for treatment, overall time to treatment is prolonged regardless of the use of POC viral load assays. • The majority of currently available POC HCV RNA assays have high sensitivity and specificity and LoD similar to lab-based assays. POC NAT assays can also be used both for HCV diagnosis and as a test of cure. • POC molecular platforms are already in use for a number of other infectious diseases, including TB and SARS-CoV-1. The availability of multi-disease testing devices offers potential for integration of HCV RNA testing that may further expand access while achieving significant system efficiencies and cost-savings.
Costing and cost–effectiveness	Two studies undertook robust cost-effectiveness analysis and found POC HCV RNA assays to be cost–effective compared with lab-based HCV RNA assays *(24-27)*.
Acceptability, values and preferences	In a multi-country online survey of 210 people in 49 countries undertaken by the World Hepatitis Alliance and Coalition Plus, there was a strong preference (93% of respondents) to do both the initial antibody screening test and confirmatory viral load test at the same place, largely for reasons of convenience, and where possible on the same day (88% of repondents). The main reasons given were the opportunity to more rapidly confirm diagnosis (81%) and start treatment (76%).

Equity	POC NAT assays have been shown to increase uptake of HCV RNA testing and treatment compared with lab-based assays, especially among people who inject drugs, homeless populations and among prisoners.
Feasibility	POC testing programmes using similar platforms have been successfully deployed in multiple countries for other uses, such as HIV EID testing, HIV viral load monitoring and TB diagnosis. Countries with existing multi-disease platforms for HIV VL testing or TB, and those that are planning for their introduction, may consider collaboration and integration of HCV VL testing.

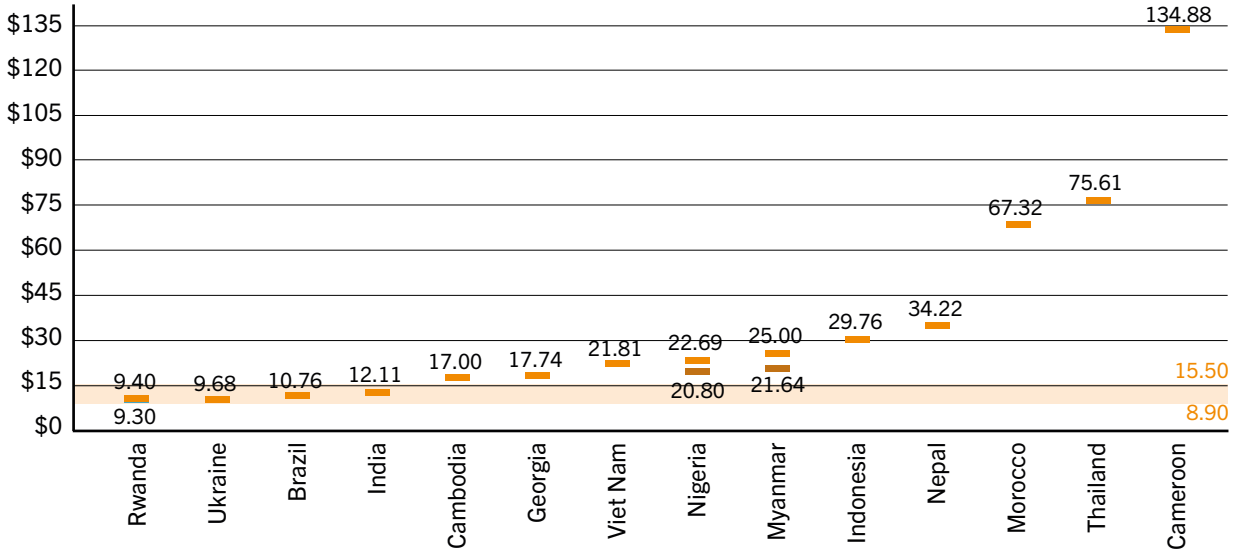
Implementation considerations – use of POC HCV RNA testing versus lab-based HCV RNA assays

- **Use of lab-based versus POC HCV RNA NAT platforms:** The decision whether to use POC or lb-based HCV RNA NAT assays depend on a variety of factors, including cost and ease of use and the characteristics of the testing site, for example, storage facilities, infrastructure, level of staff skills and cost. Use of POC assays may also be considered in services caring for specific vulnerable populations, such as people who inject drugs or people in prisons, with high loss to follow-up or in remote locations. Although POC assays may promote and expedite confirmation of viraemia, there are also many excellent examples in which a centralized laboratory-based system has been highly effective when supported by efficient sample transport and rapid electronic delivery of results.
- **Priority settings for placement of HCV POC platforms** are likely to be where there are populations at high risk of loss to follow-up and at risk of greater morbidity, but where testing volume is not large, such as at harm reduction sites for people who inject drugs, in prisons or rural settings *(24, 28-31)*.

The best results for use of POC assays were when they were placed where HCV testing and treatment were available at the same site.

- **The optimal placement of a POC instrument is where testing and treatment are at the same site or "one-stop shops".** Use of POC platforms may not achieve expected outcomes if other aspects of the care pathway require patients to travel to another clinic for treatment, with associated transport and other costs. The evidence review showed that the best results for use of POC assays were when they were placed in clinics where HCV testing and treatment were available at the same site, particularly at harm reduction sites for people who inject drugs.
- **Multi-disease testing platforms and diagnostic integration across programmes.** The introduction of multi-disease testing platforms (for HIV, TB, SARS-CoV-2, HCV), both high-throughput lab-based and POC devices, creates additional opportunities for integration that may further expand access and achieve significant system efficiencies and cost-savings. Countries with existing multi-disease testing platforms for HIV viral load or TB testing, and those that are planning for their introduction, can consider collaboration and integration of HCV RNA testing *(32)*.
- **Resource considerations:** Programmes report various final costs for HCV RNA assays (Fig. 8.1), with many LMICs paying around US$ 10 to $ 30 per HCV RNA test (both centralized laboratory-based and POC testing). The device costs as well as costs associated with operational components should also be considered. Programmes with higher volumes and pooled procurements (including with other disease assays) may achieve lower costs. In the future, increased competition may both increase access and decrease prices.

FIGURE 2 HCV RNA price per test in US$ paid by public programmes



Data collected in 2020–2021 as final prices paid by public programmes for any HCV VL assay (POC or centralized)

Source: Clinton Health Access Initiative. HCV market intelligence report, 2021 *(38)*.

Operational considerations for use and maintenance of POC RN assays

- **Both centralized laboratory and POC RNA NAT testing require strong decentralized systems** (for example, quality control assurance, platform service and maintenance, supply chain, trained staff, ongoing mentorship and waste disposal). Planning for the use of POC technologies in particular should consider how sample collection, sample processing and results return can be integrated into the patient care pathway.
- The **infrastructure** required for POC platforms will depend on the device and assay and should be reviewed and installed prior to implementation. Near-POC technologies will generally require a sturdy table for centrifugation (not required for fingerstick), air-conditioning for temperature control, a room with a sealed door to minimize dust, clinical waste disposal bins and access to a sink with running water for basic laboratory cleaning and accident management. If electricity is unstable and interrupted, an online uninterruptable power supply and voltage stabilizer are required for the Xpert device.
- **Regular internal quality control (IQC) and external quality assessment (EQA)** check to ensure that the assay works properly (quality control) and that the testing service can return the correct result (external quality assessment).
- **Staff training.** POC assays require training specific to the device used, but laboratory experience is not necessary.
- **Transport and disposal.** Assays should be transported in conditions similar to storage conditions and disposed of using proper waste management procedures, ensuring that harmful chemicals are not released into the environment. (For example, Xpert cartridges require high-temperature incineration.)

HCV DIAGNOSTICS: LABORATORY-BASED REFLEX TESTING AND CLINIC-BASED REFLEX SAMPLE COLLECTION FOR HCV RNA TESTING

Recommendations: Reflex HCV RNA testing

We recommend reflex HCV RNA testing in those with a positive HCV antibody test result as an additional key strategy to promote linkage to care and treatment.

This can be achieved either through **laboratory-based reflex HCV RNA testing** using a specimen already held in the laboratory or **clinic-based reflex specimen collection** in a health facility through immediate specimen collection following a positive HCV antibody RDT.

(conditional recommendation, low quality of evidence)

Background

A key barrier to HCV treatment following a positive HCV antibody test remains lack of access to an HCV RNA test to confirm active HCV infection and need for treatment. As a result, a significant proportion of those who test positive initially never confirm their diagnoses or link to subsequent care and treatment. One potential way to accelerate access to HCV RNA testing is by implementing reflex testing. Reflex testing, whether lab- or clinic-based, has the potential to improve outcomes across the HCV continuum of care, with increased uptake and reduced time to HCV RNA testing, increased linkage to care, increased uptake and reduced time to treatment. It also eliminates the time, inconvenience and cost of additional clinic visits. Clinic-based reflex sample collection may be further facilitated by access to POC HCV RNA assays.

Reflex testing – definitions

We define reflex testing as a linked HCV RNA NAT (or HCVAg) test that is triggered among all people who have an initial positive HCV antibody screening test result. Reflex HCV RNA testing may be implemented in two ways: either laboratory-based reflex testing or clinic-based reflex testing.

- **Laboratory-based HCV reflex testing** refers to a testing algorithm in which patients have only a single clinical encounter and one blood draw or specimen for an initial laboratory-based HCV antibody test (in some cases it may be divided in two tubes), which is then sent to the lab. If the sample for HCV antibody testing in the lab is positive, then the same existing or duplicate sample is automatically used for a prompt "reflex" laboratory-based HCV RNA (or HCVAg) test. The result returned to the patient/doctor is, therefore, for both the HCV antibody result and, if that is positive, the HCV RNA result. No further visit or specimen collection is required.
- **Clinic-based reflex testing** refers to a testing algorithm where there is only a single clinical encounter/visit for an initial rapid diagnostic HCV antibody test, but with two blood draws. A fingerstick specimen is first taken and tested using a rapid diagnostic HCV antibody test, which, if positive (after usually a 15-minute wait), is then immediately followed by a "reflex" second blood specien collection (either venous blood specimen or fingerstick) for HCV RNA detection of current infection. The second blood specimen for HCV RNA testing may either be sent to a laboratory for HCV RNA (or HCVAg) test or tested onsite using a POC HCV RNA assay.

Summary of the evidence

A WHO-commissioned systematic review and meta-analysis evaluated whether laboratory-based and clinic-based reflex HCV RNA testing reduced turnaround time between HCV antibody screening and HCV RNA testing, linkage to care and treatment when compared with the standard multi-step approach for HCV RNA testing. A total of 51 studies were included, of which nine were from LMICs and 42 were from high income countries. We categorized and analysed separately laboratory-based reflex testing and clinic-based reflex sample collection testing **(see box, Definitions)**. Of these studies, 32 were categorized as using laboratory-based reflex testing, and 19 were categorized as using clinic-based reflex specimen collection. Nine of the 32 laboratory-based reflex testing studies also had a non-reflex comparator arm, while none of the clinic-based reflex specimen collection had a comparator arm.

Laboratory-based reflex testing

Uptake of HCV RNA testing, linkage to care and treatment initiation. Overall, 95.7% (95% CI: 92.1–98.3%) of those testing HCV antibody-positive had an HCV RNA test using laboratory-based reflex testing, and 77.3% (71.3–82.8%) of those testing positive were linked to care. In studies of laboratory-based reflex testing versus non-reflex testing, reflex testing significantly increased the uptake of HCV RNA NAT testing among those testing HCV antibody-positive (pooled RR of 1.35 (95%CI: 1.16–1.58) (based on nine studies) and improved linkage to care (pooled RR of 1.47 (95% CI: 0.81–2.67) (based on five studies).

Turnaround time. By definition, the turnaround time from antibody test to sampling for reflex testing (either laboratory or clinic-based) was 0 days.

Clinic-based reflex sampling and testing

Uptake of HCV RNA testing, linkage to care and treatment initiation. In the clinic-based reflex sampling/testing studies, 93.7% (95% CI: 85.1–99.0%) of HCV antibody-positive persons had HCV RNA testing; 74.8% (27.7–100%) were linked to care, and 83.4% (79.2–87.2%) initiated HCV treatment. None of the clinic-based reflex testing studies had a non-reflex comparator arm.

Turnaround time for clinic-based reflex testing. Overall, 13 studies reported the turnaround time from RNA sample collection to HCV RNA testing. The median turnaround time was 0 days in 10 of these studies, one day for two studies and five days for one study.

Rationale for recommendations

The Guideline Development Group made a conditional recommendation for the adoption of HCV RNA reflex testing (either laboratory-based or clinic-based) as an additional strategy to promote uptake of HCV RNA testing following a positive HCV antibody test and so to promote linkage to care and treatment initiation. This recommendation was based on evidence of low certainty that reflex testing significantly increased the uptake of HCV RNA testing. There was also a non-significant increase in linkage to care and some evidence of reduced turnaround time to treatment initiation with both laboratory-based reflex testing and clinic-based reflex testing compared with routine laboratory-based non-reflex testing strategies.

Topic	Rationale for recommendation
Balance of benefits and harms	Key benefits include: • Compared with standard laboratory-based HCV RNA testing, reflex testing or one-time sample collection simplifies the care pathway and reduces the need for additional clinic visits and time to HCV RNA viral load testing and linkage to care. • Evidence that reflex testing significantly increased the uptake of HCV RNA testing and linkage to care and some evidence of reduced turnaround time to treatment initiation when compared with routine laboratory-based non-reflex testing strategies. • Reflex testing avoids the need for additional venepuncture and blood draws, which may be preferable particularly to persons who inject drugs, who are more likely to have compromised veins for blood sampling. • Based on the programme survey and cost analysis reported by Public Health England, laboratory-based reflex testing is cost-saving, feasible to implement and has the potential for widespread adoption, even in resource-limited settings, to promote HCV testing and treatment uptake.
Costing and cost–effectiveness	All respondents to the laboratory-based reflex survey across laboratory programmes reported that reflex testing was cost-saving compared with conventional two-step testing, even in the absence of formal economic evaluations. Savings were the result of reduced numbers of clinic visits and clinician time. There is potential for further savings, as one specimen could be used to test for multiple pathogens, such as HBV and HIV, on high-throughput laboratory machines.
Values and preferences	In a multi-country online community survey of 210 users of hepatitis services in 49 countries, 88% of participants confirmed a strong preference to “have the initial HCV antibody and confirmatory HCV RNA tests on the same day”. The main reasons given were the possibility to more quickly to confirm diagnosis (81%) and start treatment (76%). There was also a strong preference, for doing both the initial antibody test and confirmatory HCV RNA testing at the same place, for reasons of convenience, and at a community-friendly site. A further consideration in favour of HCV reflex testing is that, persons who inject drugs may prefer a testing strategy that requires only one blood draw.
Equity	Overall, strategies to promote uptake and linkage to care, such as laboratory or clinic-based reflex testing, will likely further promote equity in access if used in settings and populations at high risk of loss to follow-up. Populations who will particularly benefit from the convenience of a single sample collection approach include the homeless, people who inject drug and people in prisons.
Feasibility	Laboratory-based reflex HCV viral load testing is already performed routinely in many laboratory services in high-income countries. Clinic-based reflex testing following a positive HCV antibody RDT is also common practice now in low-income countries.

Implementation considerations

Choice of laboratory-based reflex testing or clinic-based reflex HCV RNA testing for different country contexts

Countries should incorporate routine reflex HCV RNA NAT testing into their national testing guidelines and testing infrastructure. The choice between laboratory-based reflex testing and clinic-based reflex testing with POC HCV RNA NAT tests will depend on national testing policies, budgets, infrastructure and human resources, as well as the extent of reliance on centralized high-throughput laboratories, the available sample transport network and location of testing and treatment services. To meet the needs of different populations or regions in a country, a mix of clinic-based and laboratory-based reflex testing strategies may be optimal.

- **A laboratory-based reflex testing approach** will be more appropriate in settings with large testing volumes supported by extensive specimen transport networks.
- **A clinic-based reflex sample collection approach to HCV RNA testing** may be preferred for populations such as key populations (particularly, people who inject drugs and men who have sex with men) and in primary care settings, where RDT testing is widely used.

Key steps to initiate laboratory-based and clinic-based reflex HCV RNA testing

1. Train outpatient clinic phlebotomy and laboratory staff on new procedures for specimen collection and processing of HCV RNA tests.
2. Update electronic laboratory order forms for anti-HCV and RNA testing to list reflex-only testing options, and develop laboratory guidance for HCV RNA reflex testing.
3. Design the laboratory process to preserve specimen integrity and limit risk of cross-contamination.
4. Plan for additional costs as needed, that is, additional tubes, transport and storage, if collecting two tubes for anti-HCV and NAT or cAg testing.
5. Combine laboratory-based reflex HCV RNA testing with other strategies, for example, clinic-based reflex testing, to meet the needs of different populations.
6. Evaluate HCV laboratory-based reflex RNA testing programmes, providing feedback to providers and lab managers for quality improvement.

* Persons with HCV genotype 3 infection who have received interferon and/or ribavirin in the past should be treated for 16 weeks.

** May be considered in countries where genotype distribution is known and genotype 3 prevalence is <5%.

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Global Hepatitis Programme
World Health Organization
Department of Global HIV,
Hepatitis and Sexually Transmitted
Infections Programme

20, avenue Appia
1211 Geneva 27
Switzerland

E-mail: hepatitis@who.int

www.who.int/health-topics/hepatitis

9789240052697