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# HIV and Hepatitis Testing: Global Progress, Challenges, and Future Directions

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## Abstract

***HIV infection and viral hepatitis due to HBV and HCV infection are major causes of chronic disease worldwide, and share some common routes of transmission, epidemiology, initial barriers faced in treatment access, and in strategies for a global public health response. Testing and diagnosis of HIV, HBV, and HCV infection is the gateway for access to both care and treatment and prevention services, and crucial for an effective HIV and hepatitis epidemic response. In this review article, we first summarize the common goals and guiding principles in a public health approach to HIV and hepatitis testing. We summarize the impressive global progress in HIV testing scale-up and evolution of approaches, with expansion of provider-initiated testing and counseling in clinical settings (particularly antenatal and tuberculosis clinics), the introduction of more community based testing services, and use of rapid diagnostic tests enabling provision of same-day test results. However, 46% of all people living with HIV are still unaware of their serostatus, and many continue to be diagnosed and start antiretroviral therapy late. As testing and treatment scale-up accelerates for an "treat all" approach, other challenges to address include how to better focus testing and reach those yet undiagnosed and most at risk, especially key populations, men, adolescents, and children. We summarize future directions in HIV testing to speed scale-up and close gaps that are addressed in the WHO 2015 consolidated HIV testing guidelines. In contrast to HIV, action in hepatitis testing and treatment has been fragmented and limited to a few countries, and there remains a large burden of undiagnosed cases globally. We summarize key challenges in the hepatitis testing response, including lack of simple, reliable, and low-cost diagnostic tests, laboratory capacity, and testing facilities; inadequate data to guide country specific hepatitis testing approaches and who to screen; stigmatization and social marginalization of those with or at risk of viral hepatitis; and lack of international or national guidelines on hepatitis testing for resource-limited settings. We highlight some of the key lessons applicable to hepatitis from the experience of expansion and diversification of HIV testing approaches over the last 30 years of the HIV response; in addition to forthcoming WHO tools to support the hepatitis global response. This includes a new 2016-2020 global hepatitis health sector strategy with testing and diagnosis targets, and 2016 WHO guidelines on hepatitis testing.*** **(AIDS Rev. 2016;18:3-14)**

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## Key words

***HIV. Hepatitis B. Hepatitis C. Testing. Key populations. Diagnostics. Low and middle income settings.***

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## Introduction and global epidemiology

HIV infection and viral hepatitis due to HBV and HCV infection are major causes of chronic disease worldwide and share some common routes of transmission, epidemiology, initial barriers faced in treatment access, and in strategies for a global public health response (Table 1). At the same time, each of the viruses requires tailored treatment and preventative interventions.

The global response to HIV represents one of the great public health achievements of recent times. In 2015, there were 36.9 million people living with HIV infection, and antiretroviral treatment (ART) had reached almost 16 million, of which more than 11 million were in the African region[1,2]. As a result, the number of adults and children dying from HIV-related causes had declined by 24% between 2000 and 2014, and those newly infected with HIV by 35%[1,2]. Key populations continue to be disproportionately affected by HIV in all settings[3]. Of the estimated 1.9 million new HIV infections worldwide in 2014, approximately 40% are estimated to occur among key populations, including adolescents, and in many settings young people are at greater risk of HIV acquisition than older people[1-3].

Worldwide, approximately 240 million people have chronic HBV infection, defined as persistence of hepatitis B surface antigen (HBsAg) for six months or more[4], and 184 million have chronic HCV infection based on presence of antibodies to HCV[5], and together they account for about for about 1.4 million deaths per year, mainly from cirrhosis or hepatocellular carcinoma[6], a toll comparable to that of HIV and tuberculosis (TB). The number of people living with HCV is also increasing, while those living with HBV are projected to remain at current high levels for the next 40-50 years. Viral hepatitis is also a growing cause of morbidity and mortality among people living with HIV[7,8]. Current estimates are that between 5 and 25% of the approximately 36.9 million HIV-infected persons worldwide also have chronic HBV (HBsAg positive, 2.7 million) and/or HCV (another 2.3 million HCV antibody positive)[7,8].

While HIV, HBV, and HCV are blood-borne infections, the predominant modes of transmission differ[8]. Mother-to-child transmission of HBV is the major mode of transmission in high-prevalence settings, and is highest in sub-Saharan Africa and east Asia, where between 5-10% of the adult population is chronically infected[9]. Immunization remains the most effective strategy for prevention of HBV infection. Hepatitis C virus epidemics related to injecting drug use occur in all regions, with significant transmission also occurring through unsafe injections and medical procedures, and less commonly through sexual contact[10]. The most affected regions are central and east Asia and parts of north and west Africa, where many infections are caused by unsafe medical injections and other medical procedures. Additionally, even in low-prevalence areas, subpopulations such as indigenous populations, migrants, people with HIV, persons who inject drugs (PWID), men who have sex with men (MSM), transgender people, people, sex workers, people in prisons or other closed settings, experience high levels of both HCV and/or HBV infection, but overall data on burden in these populations remains more limited, other than in PWID. Comprehensive prevention strategies for both viral infections should include assurance of safe blood products, safe injection practices, harm reduction services for PWID and promotion of safe sex.

The development of highly effective, well-tolerated oral drugs with high rates of cure has revolutionized the treatment of chronic HCV infection, and there is a development pipeline of additional promising options, although high prices of new medicines remain a barrier to access in many countries. Effective treatment is also available for people with chronic HBV infection. However, treatment typically needs to be lifelong, as a cure is not yet available.

In this review article, we summarize the common goals and guiding principles in the public health approach to HIV, HBV, and HCV testing; global progress and evolution of approaches in HIV testing over the 30 years of the HIV response[11]; as well as future directions in HIV testing addressed in the WHO 2015 consolidated HIV testing services guidelines to speed scale-up and close gaps. For HBV and HCV testing, we summarize key challenges in this current early phase of the hepatitis testing response; key challenges and what can be learnt from the experience of expansion and diversification of HIV testing approaches; and scope of forthcoming WHO guidelines on hepatitis testing.

## Common goals of HIV and hepatitis testing

Testing and diagnosis of HIV, HBV, and HCV infection is the gateway for access to both prevention as well as care and treatment services (Fig. 1), and is a crucial component of an effective HIV and hepatitis epidemic response. The primary goal of testing is to identify and link infected individuals and their partners and families to appropriate care and treatment to reduce HIV and hepatitis-related mortality through use of

**Table 1. Distinctive features of epidemiology and treatment coverage of HIV, HCV and HBV**

| | HIV | HCV | HBV |
|---|---|---|---|
| Main transmission route | Sexual | Parenteral | Perinatal |
| Global burden of infection | 36.9 million | 184 million | 240 million |
| Most affected regions | Sub-Saharan Africa | Eastern Europe and Central Asia | Sub-Saharan Africa and east Asia |
| Deaths per year | 1.6 million[11] | 703,800[6] | 686,000[6] |
| % infected requiring treatment over lifetime | 95% | 60-80% | 15-40% |
| Treatment duration | Lifelong | 12-24 weeks cure | Lifelong |
| % treatment coverage among those eligible | 60-80% (but significantly lower among key populations) | < 5% | < 1% |

lifelong ART in HIV-positive persons, direct-acting curative antiviral therapy lifelong and antiviral therapy for chronic HCV and HBV infection, respectively. A further aim of testing is to link to and provide preventative interventions to reduce transmission. For HIV, this includes male and female condoms, and voluntary medical male circumcision, prevention of mother-to-child transmission (PMTCT), pre-exposure prophylaxis (PrEP), and post-exposure prophylaxis (PEP) using ART, and comprehensive harm reduction services for PWID recommended by the WHO[3]. Identification of serodiscordant couples with immediate initiation of ART to prevent transmission to the negative partner, and offering PrEP to the negative partner until the positive partner is virally suppressed have both been shown to be highly effective[12]. For hepatitis, this includes provision of hepatitis B vaccination, and implementing individual or facility level prevention measures to reduce transmission to others or acquisition.

## Common guiding principles of HIV and hepatitis testing

A public health and human rights-based approach are key guiding principles underpinning delivery of both HIV and hepatitis testing. This is particularly important as many of the populations affected by HIV or hepatitis are those often systematically excluded from access to testing, treatment, and care, such as PWID, MSM[13], transgender populations, sex workers, and people in prisons and closed settings[3]. A human rights-based approach gives attention to such concerns as health-related rights (accessibility, availability, acceptability, and quality of services), gender equality, and universal health coverage so that testing and care is provided in a supportive environment free of stigma and discrimination; expanded testing and access is fair and equitable; and testing is prioritized for those most at risk.

The WHO 5 "Cs" are principles that apply to all models of HIV and hepatitis testing and in all settings: Consent, Confidentiality, Counseling, Correct test results, and Connection (linkage to prevention, treatment, and care services)[14]. This means that HIV and hepatitis testing for diagnosis must always be voluntary, consent informed by pre-test information, and linked to prevention, treatment, care, and support services to maximize both individual and public health benefits. Mandatory, compulsory, or coercive HIV or hepatitis testing is never appropriate[14], and all testing sites should ensure client confidentiality and have ethical codes of conduct.

## Global progress in HIV testing: Expansion and diversification of approaches

Over the past 30 years there has been a progressive increase in uptake and coverage of HIV testing and an evolution in testing approaches, especially in recent years. In 2014, approximately 150 million people (total of 600 million between 2010 and 2014) aged 15 years or older took an HIV test in 122 low- and middle-income countries according to the Global AIDS Response Progress Reporting (UNAIDS, UNICEF, WHO)[2]. Over a four-year period (2009-2013), there was a 33% increase in number of people tested, based on data from

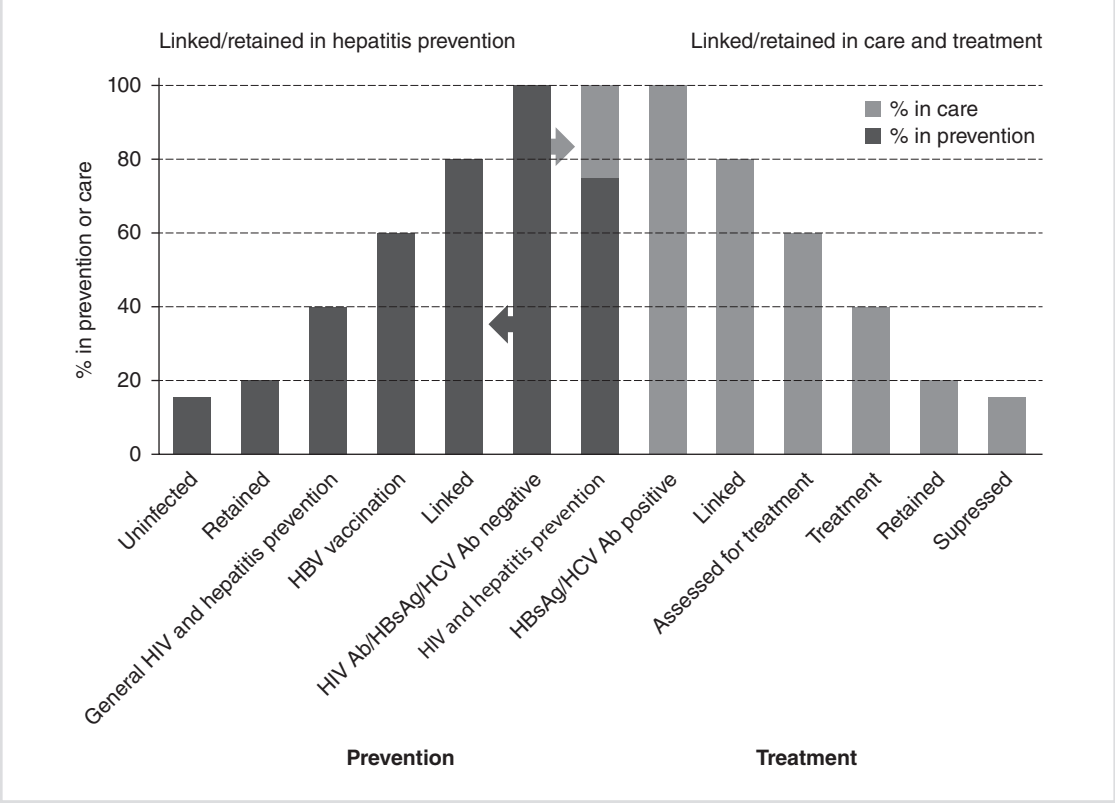


**Figure 1.** *HIV and hepatitis testing at the core of the prevention and treatment cascades* (adapted from Frits van Griensven, 2014 Thailand).

77 reporting countries[2]. The scale-up of testing has been particularly striking in Africa. In 2005 it was estimated that only 12% of people who wished to be tested for HIV were able to do so, and household surveys in high-burden African countries reported only 10% of people with HIV were aware of their status. As of 2014, it is now estimated that globally 54% (49-58%) of people with HIV (51% in Africa) are aware of their status[15].

Much of this increase can be attributed to an expansion of provider-initiated testing and counseling (PITC) in clinical settings (particularly in antenatal and TB clinics[16]), the introduction of more community based testing services, and the use of rapid diagnostic tests (RDT) enabling provision of same-day test results[2]. This has been achieved as a result of countries progressively adopting a strategic mix of testing approaches and policies[17] (Table 1). By the end of 2014, the majority of 89 (76%) of 117 reporting countries recommended PITC in their policies (often referred to as routine HIV testing) at all clinical encounters, regardless of symptoms, and 35 (90%) of 39 countries in the WHO African region recommended PITC in antenatal clinic (ANC) settings. Reported testing coverage at antenatal and TB clinics now exceeds 80% in several high HIV burden sub-Saharan African countries[17], and PITC is also being increasingly offered in pediatric in- and outpatient settings[19,20].

The majority of countries now offer rapid HIV testing with same-day results in at least some settings[2], 85 (71%) of 119 countries recommend community based testing, and 61 (53%) of 115 countries recommend lay provider testing using RDTs. Community based testing using RDTs is also becoming more widespread, particularly in the African region[21], and may involve a range of different approaches that include: home-based or house-to-house testing; campaigns linked with other screening programs such as for malaria or non-communicable diseases, e.g. hypertension; and outreach, mobile or workplace screening programs. Such programs have proved highly acceptable and effective in reaching large numbers of first-time testers and people who do not typically use health services,

**Table 2. Policies and practices related to HIV testing in low- and middle-income countries, 2013**

| | National HIV testing and counselling policy or guidelines | | | | |
|---|---|---|---|---|---|
| | Ensure provider-initiated testing and counselling in all patient | Address HIV testing and counselling for key populations | Address HIV testing and counselling for adolescent | Support rapid testing with same-day results | Support HIV testing and counselling provided by community |
| Yes | 89 | 113 | 100 | 109 | 85 |
| No | 20 | 5 | 14 | 7 | 28 |
| Other | 8 | 1 | 5 | 3 | 6 |
| Countries reporting | 117 | 119 | 119 | 119 | 119 |

Source: Global AIDS Response Progress Reporting (UNAIDS, UNICEF, WHO) 2013[17].

and in diagnosing people at earlier stages of HIV infection and linking them with care[22].

## Continuing challenges in HIV testing

Despite significant global progress in the uptake of HIV testing, approximately half of all people living with HIV are still unaware of their serostatus, and many continue to be diagnosed and start ART late. Current testing approaches are also not targeting and reaching sufficiently those people most at risk in key populations (PWID, MSM, transgender people, sex workers, and people in prisons and closed settings), and those as yet undiagnosed, a situation that has changed little in the last 15 years. Although in 2014, the majority of reporting countries stated that their national HIV testing policies addressed key populations and adolescents, actual implementation has been limited. Specific challenges include the following:

### *Low coverage rates in key populations, adolescents, children, and men*

#### Key populations

Key populations continue to be disproportionately affected by HIV in all settings[3,23,24]. Pooled HIV prevalence is 10-50 times greater than in the general population, and of two million new HIV infections worldwide in 2013, an estimated 40% of adult infections occurred among key populations[23,25]. Despite this high HIV burden, testing coverage as well as linkage to care among these populations remains low[25]. Reasons include their experience of stigma and discrimination or criminalization of their behaviors, which hinders access to health services[3,26]. Furthermore, mandatory or coerced testing, especially among prisoners[27] and migrants[28], is also still being reported. To reduce HIV burden, access for key populations with tailored testing approaches should be prioritized by countries.

#### Adolescents

Uptake of testing as well as linkage and retention in care is particularly poor among adolescents, especially girls; fewer than one in five girls aged 15-19 years were aware of their HIV status, based on Demographic Health and other surveys conducted between 2008 and 2012 in the WHO African region[29]. Adolescent services remain limited or of poor quality, so there has been little support in overcoming barriers in access to testing and care.

#### Children

HIV testing coverage among children also remains low. In many settings, PITC is rarely offered to children in clinical settings, even in countries with generalized epidemics[30-32]. Although testing coverage in PMTCT programs has improved significantly over the past decade, still only one-third of infants born to HIV-infected mothers received a virological HIV test within the first two months of life in 2012[29]. Such low HIV testing coverage for infants and children represents a missed opportunity to offer HIV testing to parents, caregivers, and family members of children. In order to improve health outcomes and survival in children, approaches are needed to increase early infant diagnosis and timely referral of HIV-positive infants to care and treatment.

### Men

Overall, men are less likely than women to test and know their HIV status; women comprised about 69% of adults who were HIV tested in 2014 in low- and middle-income countries[15,33,34]. This is largely because testing is still mainly conducted in antenatal services (ANC), even in low and concentrated epidemics[33,35]. This highlights the need for strategies that increase men's uptake of HIV testing, including provision of testing in settings that are more acceptable and accessible to men.

### *Missed opportunities for provider-initiated HIV testing and of index partner and couples*

Despite high levels of acceptance and increasing uptake of PITC in ANC and TB clinics, there remain many missed opportunities to offer HIV testing in other clinical settings, such as sexually transmitted infection clinics, primary care, and pediatric in- and out-patient settings. HIV testing coverage even among pregnant women is still less than 40% in Asia and some African countries[2]. In addition, although cohabiting relationships and HIV serodiscordancy are common[36-38], and 80% of countries in the African region include partner testing in their national policies, it has not been widely implemented, and HIV testing rates for couples in ANC settings are very low and exceed 20% in only a few countries. Rwanda is an exception, where 85% of partners are tested in ANCs. Failing to offer couples and partner testing for people with HIV is a missed opportunity as this is a high-impact approach that has the highest positivity rate of any testing approach based on a recent systematic review in sub-Saharan Africa[39]. Also, a cost-effectiveness analysis of various high-throughput screening approaches in Mozambique, Nigeria, and Senegal showed that index partner testing would identify the greater number of new HIV-positive cases, but require few resources compared to most other approaches[40].

### *Late or delayed linkage to prevention, treatment, and care*

Around one quarter of people with HIV are diagnosed late (defined as late presenters) when their CD4 count is already below 200 cells/µl and therefore initiate ART too late to get the full benefit of treatment. The proportion has not decreased significantly over the past decade and is highest among people infected through injecting drug use[41]. The proportion of individuals who are lost to follow-up between diagnosis and ART initiation also remains high in many countries (around 40% in sub-Saharan Africa)[15,42,43], and among children[17,44]. Barriers that impede linkage to HIV care include transport costs and distance to the facility, stigma, fear of disclosure, and long waiting times and delays in ART initiation[17,45], as well as various policy and legal barriers that may hinder access particularly for key populations. A combination of interventions are needed to improve linkages and reduce loss to follow-up between HIV testing and treatment and care, especially for key populations.

### *Misdiagnosis of HIV and quality of testing*

There are growing concerns about the quality of HIV testing, with reports of significant rates of false-positive diagnoses, ranging from 2.6 to 10.3% in selected countries in sub-Saharan Africa[46,47]. The most serious consequences of a misdiagnosis include unnecessary initiation of life-long ART in those with a false-positive result, and potential transmission risk to partners and infants in those with a false-negative diagnosis. Such misdiagnoses due to poor quality HIV testing may result from a combination of factors, including improper use of the testing strategy and/or algorithm or of storage of test kits and supplies, poor product performance, clerical or transcription errors, user errors in performing the test and/or interpreting the test result, and lack of supportive supervision and training. In a recent policy analysis of 48 countries, less than 20% of national HIV testing strategies aligned with the WHO recommended testing algorithms[14]. Effective quality assurance systems are needed alongside expansion in delivery of testing to address these issues.

## Future directions in HIV testing to accelerate scale-up and close gaps

### *Global targets for HIV testing*

The 15.8 million people receiving ART in 2015 ranks among the great public health achievements of recent times. The next challenge is to accelerate the scaling up of testing and treatment so that ART is available to "treat all" 36.9 million people living with HIV, i.e. doubling the number of people who were receiving ART in 2015, as recommended in the 2015 ARV guidelines[48]. The United Nations Program on HIV/AIDS (UNAIDS) and the WHO have endorsed new global Fast-Track 90-90-90 targets that call for 90% of all people with HIV to be diagnosed, 90% of people diagnosed with HIV to receive ART, and 90% of those on ART to have a

suppressed viral load by 2020[42]. Achieving the first 90 target, together with earlier diagnosis and addressing other gaps in coverage and access for key populations, will require testing programs to become even more focused and strategic.

## *2015 WHO consolidated HIV testing guidelines*

In 2015, the WHO published consolidated HIV testing guidelines that provide comprehensive guidance on HIV testing for use by national program managers and service providers in planning testing programs in a variety of settings, contexts, and diverse populations[14]. These guidelines brought together existing WHO guidance on HIV testing[3,49-54] with new recommendations on community based testing by trained lay providers, and on improving the accuracy and quality of test results. The guidelines also offered guidance to countries on how to deliver a mixture of testing approaches according to their epidemic context, focusing on testing groups most affected and currently undiagnosed and underserved. The guidelines also highlight the need for tailored testing approaches for key populations, infants, children, adolescents, pregnant and post-partum women, couples, and partners.

### Strategic mix of different HIV testing approaches

Countries need to consider a strategic mix of facility based and community based HIV testing approaches to reach different populations, diagnose people earlier, and link them to prevention, treatment, and care. Different testing approaches include: expansion of routine facility based testing to other clinical settings beyond ANC and TB, such as sexually transmitted infection clinics and primary care; indicator condition testing, index partner, couples, and family testing (one of the most efficient ways of identifying people with HIV, and in particular encouraging testing of male partners in all settings[14]); and expanding community based testing services offered through home-based outreach, in schools and other educational establishments[21] as well as in workplaces, and, potentially, HIV self-testing (HIVST).

The selection and mix of testing approaches by countries should be based on a review of their specific epidemiological situation (e.g. HIV prevalence, populations and geographic areas most affected and currently undiagnosed), current coverage of testing and treatment, and available financial and human resources[52]. Testing approaches also need to be tailored for specific population groups to, for example, overcome current reluctance for partner testing; make services more acceptable and accessible to men and key populations; diagnose HIV-exposed infants as early as possible through virological testing; and test children and adolescents not reached through infant testing programs. There is also a need for strategies to increase the offer of and uptake of couples and partner testing, particularly among index cases.

### Legitimize lay provider testing

The 2015 guidelines recommended that lay providers who are trained to use rapid diagnostic tests can independently provide HIV testing services[14]. This is based on consistent evidence that provision of HIV testing by trained lay providers is as accurate as testing by laboratory staff and healthcare providers; can both increase access and uptake among key populations and other priority groups who may be reluctant or unable to access HIV testing services in health facilities and; cost less than using other health workers to perform the same tasks.

Successful implementation of testing by trained lay providers requires countries to consider appropriate selection, training, and mentoring including regular external quality assessment; adequate remuneration; and necessary changes in policies or regulations so that lay providers can provide a full range of HIV testing services, including collecting specimens, performing rapid tests, giving pre-test information and post-test counseling, and supporting linkages to prevention, care, and treatment services.

### Expanding community based testing through "test for triage"

"Test for triage" is an alternative, simplified, community based HIV testing approach now recommended by the WHO that responds to concerns that complex testing algorithms may lead to errors[55]. This approach is already being offered by many NGOs and other community based organizations, and involves a single rapid diagnostic test offered in the community with linkage to further testing in a facility to confirm an HIV-positive diagnosis and initiate clinical care and ART.

Key advantages of this "test for triage" approach are that it should improve access for those at highest risk and not currently testing for HIV; simplify the work of lay providers; and reduce logistics, supply chains, and training. Potential challenges are: communicating correctly the

meaning of a reactive "test for triage" result; the higher rate of false-reactive test results especially in low prevalence settings; and challenges in linkage and tracking of clients to additional testing to confirm the HIV diagnosis[55].

## HIV self-testing: An emerging strategy

HIV self-testing is another emerging approach, where an individual performs an HIV test and interprets his or her own results in private. Although all reactive self-test results must be confirmed with a further test, the convenient and private nature of HIVST may help expand testing, especially among people who might otherwise not test because they are reluctant to use existing services or who frequently retest[14]. The current evidence remains limited, and there are no formal WHO recommendations on HIVST. A recent review reported high levels of acceptability of HIVST among key populations, especially MSM[56-58], increased uptake, with good accuracy (sensitivity as high as 98% and specificity as high as 100%)[59], and linkage to care using proactive intervention such as home-based care or active community based follow-up[50,54], and no major adverse events or harms due to HIVST, such as suicide or self-harm[60].

HIV self-testing is available formally and informally in several low- and middle-income countries[61]. Several countries have developed or are planning to introduce policies on HIVST, and many have embarked on demonstration projects to identify effective, acceptable, and ethical approaches to deliver HIVST in different populations and settings [62,63], such as the STAR study in Malawi, South Africa, Zambia, and Zimbabwe which will inform planned WHO HIVST guidance in 2016.

## Improving quality of testing and preventing misdiagnosis

Key steps to improve the quality of HIV testing and minimize misdiagnoses and their associated medical, social, and psychological consequences include having appropriate quality assurance and quality improvement mechanisms in place[64], and following WHO-recommended testing strategies and validated national testing algorithms, that includes retesting all people diagnosed with HIV before initiating ART[65]. While routine retesting is recommended for people at high ongoing risk of exposure[26], offering retesting to HIV-negative people at low ongoing risk is now considered unnecessary and an ineffective use of resources.

## Improving linkage to care

The 2015 WHO testing guidelines outline proactive approaches for countries to strengthen referral and linkage procedures between testing and prevention, treatment and care services, and remove unnecessary delays before initiating ART. The effectiveness of linkage varies across different high-throughput screening approaches. While linkage may generally be easier with facility based compared to community based testing, not all facilities have successful follow-up and, conversely, high levels of linkage in community settings can be achieved with more intensive support. As more countries move towards initiating ART regardless of CD4 cell count, the phase of pre-ART care should become less important and linkage to ART would be expected to strengthen.

# Hepatitis B and C testing: Current challenges

## *High burden of undiagnosed infection and late diagnosis*

Despite the high global burden of disease due to chronic hepatitis B and C, and the major opportunities with advances in highly effective "curative" oral treatment for chronic HCV infection and effective long-term with tenofovir for HBV infection, to date action has been fragmented and limited to a few countries. One of major obstacles to action is the large burden of undiagnosed cases globally; it is estimated that less than 5% of people with chronic HBV or HCV infection know their status. This contrasts with the considerable recent progress in HIV testing coverage such that now more than half of people living with HIV are aware of their status globally.

The extent of this hidden burden is poorly documented, and largely based on limited data from higher income settings. Around 15% of those chronically infected with HCV and around one quarter of those with HBV were reported to be aware of their diagnosis, based on studies from the USA, Europe, and China[66-68]. However, in low-income settings only a tiny fraction (< 1%) are likely to be aware of their diagnosis. As a result of this lack of awareness of status, they also tend to present late with advanced disease. Early identification of persons with chronic HBV (or HCV) infection would enable infected persons to receive necessary care and treatment to prevent or delay onset of liver disease, and with HBV, screening to identify and vaccinate susceptible household contacts and sex partners to interrupt ongoing transmission.

### *Key barriers in access to and uptake of testing*

There are several reasons for current very low rates of hepatitis testing in low- and middle-income countries. These reflect some of the same initial barriers to HIV testing and treatment access at the start of the global response, and include limited data on the epidemiological situation, high levels of stigma and discrimination, cost of diagnostic assays, complexity of screening, treatment, and follow-up monitoring, lack of political and financial commitment, highly specialized vertical services, and limited patient and community engagement. Specific barriers include:

- Lack of healthcare infrastructure or facilities for testing, that can reach most affected and vulnerable populations, including harm reduction services for testing.
- Limited access to reliable and low-cost HBV and HCV diagnostics, including rapid serological tests and molecular viral load tests that are quality assured by stringent regulatory authorities, including WHO, and poor laboratory capacity. In addition, few low- and middle-income countries have ready access to additional tests to stage liver disease and guide treatment decisions, such as transient elastography.
- Weak hepatitis surveillance programs, and limited national and subnational data on the epidemiological situation to guide country specific hepatitis testing approaches.
- High levels of stigma, discrimination, and social marginalization of those with or at risk of viral hepatitis, such as PWID, MSM, prisoners, and sex workers.
- Limited access to hepatitis treatment, which remains unaffordable to those most in need, and poor linkage to care, even for those who have been diagnosed.
- Lack of awareness of as well as understanding about hepatitis B and C disease progression and treatment among patients and healthcare workers.
- Lack of testing guidance for low- and middle-income settings, and limited evidence base to guide hepatitis testing approaches. Although several international professional organizations (such as the European Association for the Study of the Liver [EASL], the Asian Pacific Association for the Study of the Liver [APASL], the American Association for the Study of Liver Disease [AASLD], the U.S. Centers for Disease Control [CDC], the United Kingdom National Institute for Health and Care Excellence [NICE]), and national authorities such as in Australia, Canada, France, Egypt, South Africa, and Switzerland have developed screening guidelines for HBV and HCV infection, these are predominantly focused on high-income settings. There have also been few large studies or randomized controlled trials of impact or cost-effectiveness of different hepatitis testing approaches to support the development of guidelines.
- Lack of political and financial commitment. Few countries have national viral hepatitis strategies or plans, and even fewer have designated units and budgets within their health ministries to lead, guide, and coordinate their hepatitis responses.

### *Hepatitis B and C testing: Next steps – What is needed?*

In order to overcome these challenges, and substantially increase awareness of hepatitis status and earlier diagnosis there is a need to provide services that can reach those populations most affected; well-functioning laboratories to ensure high-quality testing and treatment monitoring; a secure supply of quality-assured affordable diagnostics; an appropriately trained health workforce; and active involvement of affected communities. As with HIV, if hepatitis testing is to fulfill its potential as the gateway to both treatment and prevention, we need both more testing and better approaches for priority groups.

Two key WHO tools to support the global response and scale-up of hepatitis testing include a new 2016-2020 global hepatitis health sector strategy with testing and diagnosis targets, and forthcoming WHO 2016 guidelines on hepatitis testing.

## Global health sector strategy and targets on hepatitis 2016-2021.

In response to the two World Health Assembly resolutions on viral hepatitis in 2010 and 2014[69,70], together with a growing recognition of the huge public health burden of hepatitis and opportunities for action, a global health sector strategy on viral hepatitis has been developed to guide a coherent global public health response. The strategy outlines a series of impact and service delivery coverage targets towards elimination of viral hepatitis, as well as priority actions to be taken by countries and the WHO to achieve these targets. These include targets for a major increase in diagnosis of chronic hepatitis B and C for 2020 and 2030.

## 2016 WHO hepatitis testing guidelines: Future directions in hepatitis testing

Existing WHO guidelines for management of persons with chronic HBV and HCV infection provides[71,72] recommendations along the continuum of care from initial assessment, including staging of liver disease using noninvasive tests, who to treat, what treatments to use, and how to monitor, but to date there has been a lack of guidance on hepatitis testing. In 2016, the WHO will publish hepatitis testing guidelines for adults, adolescents, and children in low- and middle-income countries that will include recommendations on who to test or screen, as well as how to screen in terms of selection of diagnostic tests and strategies. These guidelines will also build on a decade of evolution in WHO HIV testing guidance that includes provider-initiated testing guidance, service delivery guidance, couples testing and home based testing, and now planned guidance on self-testing.

There are several key lessons to be learnt from the experience of HIV testing. First, that success is possible based on the exponential increase in uptake of HIV testing; second, the impact of an evolution in HIV testing approaches, and in particular the value of expanding opportunities for facility based testing beyond ANC and TB clinics to include sexually transmitted diseases clinics and primary care, as well as moving testing out of healthcare facilities into the community; third, the importance of innovative HIV service delivery approaches for marginalized and vulnerable populations that can be adapted to also reach populations most affected by viral hepatitis; and finally, the importance of involving affected populations in delivering more acceptable and effective services.

Important future directions in hepatitis testing will include the following:

- Optimizing service delivery of hepatitis testing by integrating hepatitis testing into other healthcare and testing services such as HIV and sexually transmitted infection clinics, antenatal services, drug treatment programmes and prison services to increase efficiency, reach, and acceptability; as well as expanding opportunities for community based testing to reach marginalized groups and ensure equitable access to testing. Appropriate models of integration and linkage will depend on the country context and health system.
- Adaptation of the WHO hepatitis testing guidance into national hepatitis plans and policies according to country epidemiological context and health systems that target priority populations and locations, and tailor testing approaches, depending on each country's epidemiology and context. For example, priority might be given to specific age groups (such as those born between certain dates), certain high-prevalence groups (such as incarcerated persons, people who inject drugs, migrants, hemodialysis patients, people who undergo skin-piercing procedures including tattooing, some indigenous communities, sex workers and MSM), and those with advanced liver disease.
- Strengthening national laboratory systems to provide quality diagnosis of chronic HBV and HCV infection, and a reliable supply of quality assured (eg. WHO prequalified) diagnostics, with simplification of hepatitis diagnostic pathways to ensure that testing services can reach remote areas and hard-to-reach populations. There is a need for more reliable and low-cost rapid diagnostic tests for viral hepatitis B and C, point-of-care testing for monitoring hepatitis B and C viral load (and hepatitis C antigen) to guide treatment decisions, and simplified tests for assessing liver fibrosis and cirrhosis.
- Accurate forecasting of country and global needs in diagnostic commodities. Effective testing programs rely on an uninterrupted supply of diagnostics. Robust procurement and supply management systems, such as bulk procurement, advanced purchasing, and improved forecasting are required to ensure savings on procurement of hepatitis diagnostics and introduce efficiencies in supply management.

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